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FEBRUARY 1951

VOLUME 63 NUMBER 2

Published Monthly by
AMERICAN MEDICAL ASSOCIATION
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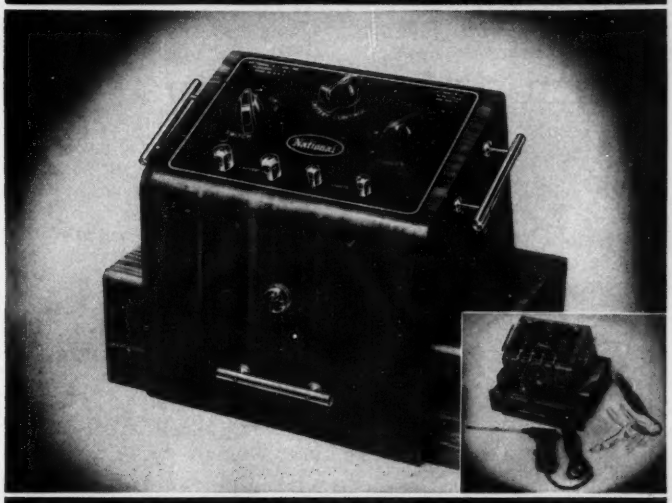

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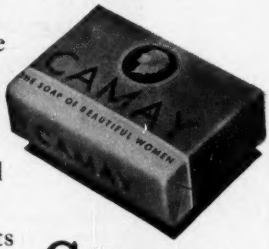

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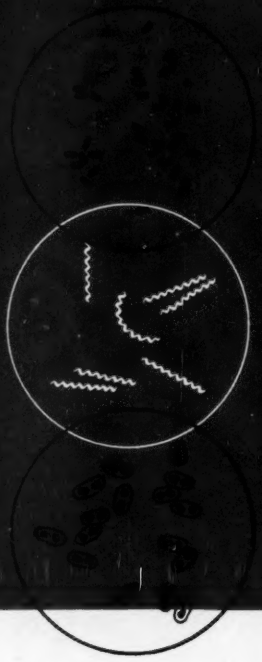

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1. Kessler, G.: Ann. N. Y. Acad. Sc. 53:221 (Sept. 15) 1950.

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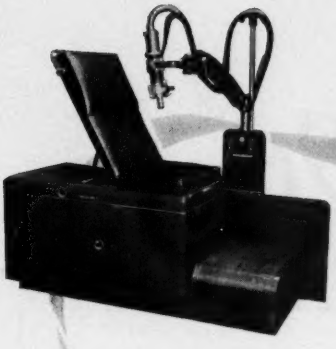

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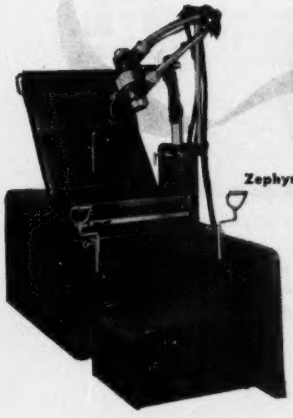

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Communications regarding subscriptions, reprints, etc., should be addressed, A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, American Medical Association, 535 North Dearborn Street, Chicago 10.

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A. M. A.
Archives of Dermatology and Syphilology

VOLUME 63 FEBRUARY 1951 NUMBER 2

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LYMPHOCYTOMA CUTIS

Report of Two Cases

ADOLPH B. LOVEMAN, M.D.
AND
MAURICE T. FLIEGELMAN, M.D.
LOUISVILLE, KY.

IN 1906 Jadassohn [1] presented before the Ninth German Dermatological Congress the first case of what was later to be known as lymphocytoma cutis. It was reported as a case of pseudoleukemic infiltration of the skin. In 1922, when discussing Biberstein's [2] case, Jadassohn commented that his original patient was still living, that the skin lesions were unchanged and that no signs or symptoms of leukemia had developed. His case was that of a young woman of 33 years of age, who presented on both cheeks symmetric semitransparent papules and nodules, varying in size from that of a lentil to that of a cherry. A clinical diagnosis of lupus tumidus was made, but the histological examination disproved the clinical impression. The section revealed an entirely lymphadenoid structure arranged in a fine reticulum. Occasional plasma and giant cells were noted.

In 1921 Kaufmann-Wolf [3] reported two cases in children and coined the name "lymphocytoma." She did not feel that the condition was related to leukemia but stated that it was a hyperplasia of the lymphatic tissue, preexisting in the skin and of unknown etiology. Since then many cases have been reported. In 1935, however, Berde and Lang [4] reported that they were able to find at that time only 35 cases in the literature. In 1935 Epstein [5] wrote a most comprehensive article reviewing the literature and reporting four cases of his own. In addition, he presented a clinical classification of the various types of lymphocytoma. In 1939

Studies and contributions from the Department of Dermatology and Syphilology, University of Louisville School of Medicine.

Read before the Section on Dermatology and Syphilology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 28, 1950.

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4. Berde, K., and Lang, M.: Über Lymphocytoma miliare cutis, Dermat. Wchnschr. **100**: 641 (June 8) 1935.

5. Epstein, S.: Lymphocytome der Haut mit Beteiligung der Conjunctiva bulbi: Beitrag zur Pathogenese der Lymphocytome, Arch. f. Dermat. u. Syph. **173**:181, 1935.

Hallam and Vickers [6] and Hellier [7] reported cases and likewise reviewed the literature to date. The latter emphasized the scarcity of reports in the British literature and stated that he had been able to find only two instances of previous reports. The most extensive monograph yet written is that of Bäfverstedt,[8] in which were reported 41 cases from Stockholm and vicinity and in which were collected 101 cases from the literature. These included many cases previously described as Spiegler-Fendt sarcoid, and, although we feel there is much to justify including such cases with the lymphocytoma group, yet such a classification may not meet with universal acceptance. The only additional report which we have encountered since that of Bäfverstedt is an article by Hargreaves,[9] in which were reported two cases occurring in children.

In spite of the many reports of cases of lymphocytoma cutis which have appeared in the foreign literature, no formal full length reports have appeared in the American literature. Only isolated case presentations at society meetings [10] have been encountered. Discussions at these meetings and personal communications [11] reveal that additional cases have undoubtedly been encountered. Mopper and Rogin [12] have recently observed three cases of solitary lymphocytomas.

It is of interest to note, however, that in spite of the fact that American dermatologists have contributed so little to this subject, it has not been entirely neglected in the American textbooks on dermatology.[13] The Suttons,[13b] in addition to discussing this entity in their several textbooks, present a classic photograph of one of their personal cases. We are indebted to one of them (R. L. S. Jr.) for lending us the histological section for study, as well as for furnishing us with a brief history of the case. Hamilton Montgomery [14] also gives a brief account of Lymphocytoma Cutis in his monograph on the lymphoblastomas for "Oxford Loose-Leaf Medicine."

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6. Hallam, R., and Vickers, H. R.: Two Cases of Miliary Lymphocytoma or Benign Lymphadenoid Granuloma of the Skin, Brit. J. Dermat. **51**:251 (June) 1939.

7. Hellier, F. F.: Lymphocytoma of the Face, Brit. J. Dermat. **51**:260 (June) 1939.

8. Bäfverstedt, B. O.: Über Lymphadenosis benigna cutis, Acta dermat.-venereol. (supp. 11) **24**:1, 1943.

9. Hargreaves, M. A.: Two Cases of Lymphocytoma, Dermatologica **99**:220, 1949.

10. (*a*) Wise, F.: Disseminated Miliary Lymphocytoma of the Face and Neck, Arch. Dermat. & Syph. **39**:749 (April) 1939. (*b*) Localized Lymphocytoma, ibid. **50**:141 (Aug.) 1944. (*c*) MacKee, G.: Lymphocytoma of the Nose, ibid. **50**:142 (Feb.) 1944. (*d*) Epstein, S.: Lymphocytoma Miliare Faciei, ibid. **59**:365 (March) 1949. (*e*) Foerster, O. H.; Foerster, H. R., and Ruch, D. M.: Lymphocytoma, ibid. **60**:874 (Oct.) 1949. (*f*) Netherton, E. W.: Aleukemic Lymphocytosis Cutis (Lymphocytoma of the Skin), ibid. **57**:779 (April) 1948. (*g*) Lentz, J. W., and Beerman, H.: Lymphocytoma Cutis, ibid. **60**:459 (Sept.) 1949.

11. Lamb, J.; Rogin, J.; Montgomery, H.; Epstein, S.; Sutton, R. L., Jr.; Bianchi, G., and Rutledge, W. U., in discussions and personal communications to the authors.

12. Mopper, Coleman, and Rogin, J. R.: Benign Solitary Lymphocytoma: Report of Three Cases, Arch. Dermat. & Syph., this issue, p. 184.

13. (*a*) Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, New York, Lea & Febiger, 1948, p. 874. (*b*) Sutton, R. L., Sr., and Sutton, R. L., Jr.: Handbook of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1949, p. 654, fig. 953. (*c*) Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946.

14. Montgomery, H.: Mycosis Fungoides, Lymphoblastoma of the Skin and Allied Conditions as General Diseases, in Oxford Loose-Leaf Medicine, to be published.

It is felt, therefore, that the following case reports are justified to call to the attention of American dermatologists an entity with which they are not overly familiar and to attempt to unravel some of the confusion and misconceptions which exist concerning this condition.

REPORT OF CASES

CASE 1.—Mrs. G. R., aged 32, was first seen by us in January 1949, complaining of a small lesion on the tip of her nose. History revealed the fact that she had had recurrent small papules on her nose and cheeks since 1942 and had been told that these were superficial skin cancers. A biopsy, however, did not confirm this clinical impression. The specimen was apparently reported as showing chronic inflammation and "granulation tissue." Previous treatment had consisted in electrodesiccation of both new and recurrent lesions, of which there had been many. The patient's general health was good, and she had no other complaints. She felt that exposure to sunlight caused pruritus in both the lesions and the scars but that it did not cause any exacerbation of her condition. The past history was irrelevant. Blood counts during each of three pregnancies were normal.

Examination and Clinical Course.—The patient presented a bluish gray semitransparent papule 4 to 5 mm. in diameter near the tip of her nose. Surrounding this was an atrophic scar,

Fig. 1 (case 1).—Small transparent papule near tip of nose.

recurrence in scar tissue thus being evidenced. Numerous atrophic scars were seen scattered over the cheeks and the nose. No other cutaneous or mucosal lesions were noted at this time. The following clinical diagnoses were entertained: (1) epithelioma adenoides cysticum, (2) lupus erythematosus and (3) keloid.

The patient was seen on numerous occasions between her initial visit and May 1950. During this period of observation a number of new lesions appeared, some on her nose and others on her cheeks and ear lobes. These varied from those about pinhead size on the ear lobes to several of 5 to 6 mm. in diameter on the cheeks.

Laboratory Data.—Several hematological examinations were made, all of which gave essentially normal results. A typical count, as reported by Dr. Marion F. Beard, hematologist, was as follows: total white blood cells, 6,400; total red blood cells, 4,430,000; total platelets, 354,000; hemoglobin, 10.5 Gm. (68 per cent); color index, .77, and differential count—84 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes and 8 per cent monocytes. Subsequent examinations revealed normal hemoglobin readings. Except for the observation of a few immature lymphocytes, the bone marrow was likewise normal, as was the condition observed on roentgenologic examination of the chest. The blood cholesterol was 144 mg. per 100 cc. of blood, and the blood Kahn reaction was negative.

At the initial visit a biopsy specimen was taken from the lesion on the nose but was unsatisfactory for accurate interpretation. Biopsies were repeated of specimens from papules on the cheeks in March 1949 and March 1950. Before the second biopsy specimen was taken

the following additional clinical diagnoses were entertained: (1) sarcoidosis, (2) lymphoblastomas, (3) unusual lipid dyscrasia and (4) atypical mucinosis. Some of the bluish slate gray, elastic-like papules even resembled the small papules seen in von Recklinghausen's disease.

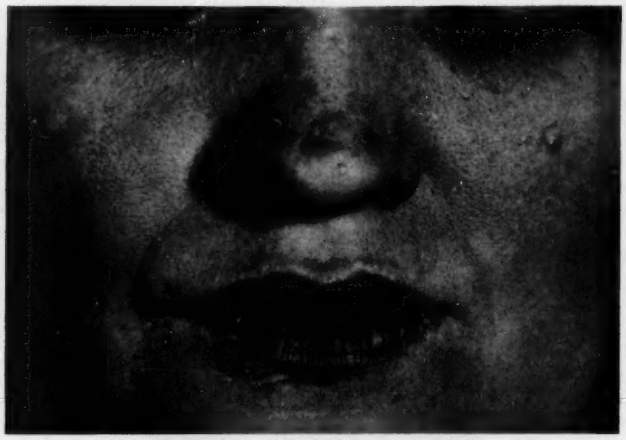

Fig. 2 (case 1).—Note miliary papule on tip of nose and papules on cheeks.

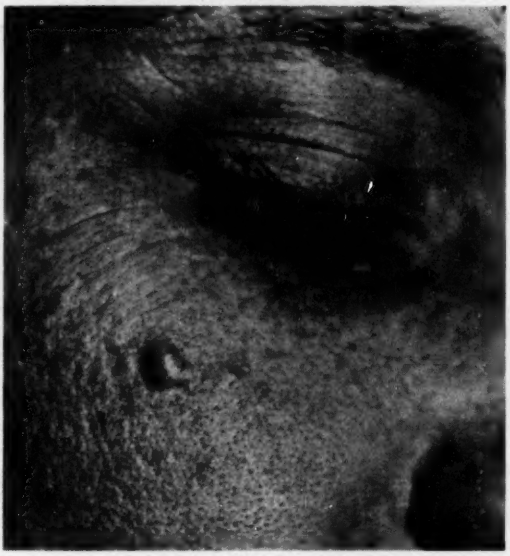

Fig. 3 (case 1).—Recurrent papule on cheek.

Histopathological Picture.—A small punch biopsy was made at the time of the initial visit in January 1949. A definite histological diagnosis could not be made then because the section was unsatisfactory. There was, however, no evidence of carcinoma. There was a fairly

extensive infiltration of small, mature lymphocytes, many of which were perivascular, but the section was too superficial and the extent and depth of the infiltrate could not be accurately ascertained. Another biopsy specimen was taken in March 1949, from the lesion on the cheek,

Fig. 4 (case 1).—Low power view of specimen. Note packing of lymphocytes forming germinal-center-like area. Note that the subepidermal zone is relatively free from any infiltration.

and Dr. Harry M. Weeter, pathologist, reported it as a tumor of the lymphoblastic series, suggestive of leukemia. We reviewed the sections and were unable to rule out the diagnosis of the circumscribed type of lymphocytoma cutis. Dr. Weeter's attention was called to this

possibility, and, after studying the sections further and reviewing the articles by Hallam and Vickers and by Hellier, he issued the following subsequent report: "Examination of the sections showed certain features characteristic of lymphocytoma of the skin. There was a thinning of the overlying squamous epithelium, an occasional dipping in of the same, with keratotic

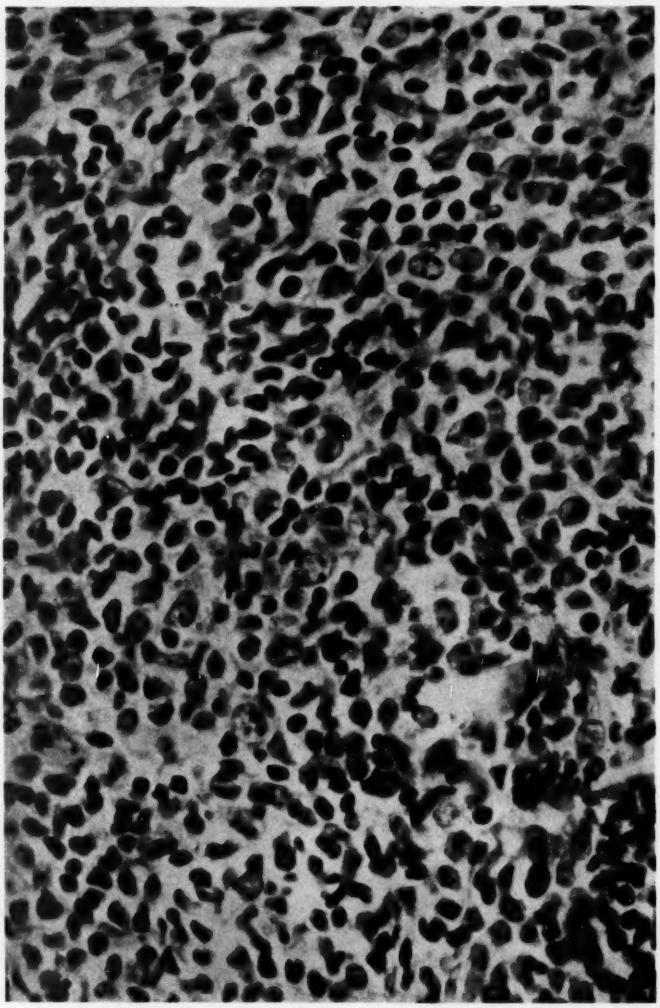

Fig. 5 (case 1).—High power view of specimen. Note the two distinct cell types: small, dark-staining lymphocytes and larger cells with pale nuclei.

plugging, and obliteration of the epithelial pegs and papillae. There was an abscence of the subdermal structures in the area occupied by the tumor cells. An unoccupied zone was noted between the epithelium and the cellular infiltrate. The nodules were composed almost

entirely of deeply staining mature lymphocytes and larger pale cells, with one, and sometimes two, nucleoli. A fine reticulum was noted in certain areas. No typical germinal centers were seen. I believe a diagnosis of lymphocytoma cutis is justified."

Dr. Stephan Epstein and Dr. John B. Miale, of the Marshfield Clinic, and Dr. Hamilton Montgomery, of the Mayo Clinic, examined the sections and concurred in the above diagnosis. Dr. Epstein called attention to the aggregation of darker-staining cells in the center of one lesion, which he felt to be quite characteristic. Dr. Miale emphasized the nodular formation of the cellular infiltrate in certain areas.

Therapy.—Various types of therapy were used in the treatment of this patient. They included superficial roentgen irradiation, destruction of the lesions with the actual cautery and the administration of arsenic trioxide, penicillin and aureomycin.[15] The most efficient therapy was superficial roentgen irradiation, in doses of 150 to 200 r, unfiltered, given two or three times, at intervals of two to three weeks. The response was extremely satisfactory. In fact, in this particular case, the lesions had practically entirely disappeared three weeks after the initial exposure and pronounced regression was noted within a week's time. Regardless, however, of the type of therapy administered, new lesions, as well as recurrences in scar tissue, were rather frequently encountered. The antibiotics were employed because Bianchi,[11] of Miescher's Clinic, was successful with penicillin therapy in certain cases of lymphocytoma cutis. After a recurrence in October 1949, 600,000 units of procaine penicillin G with aluminum monostearate were given daily, for a total dose of 10,000,000 units, with no visible effect on the lesions. In March 1949 new lesions were found over the cheeks and the nose, and in April 1950 additional ones were noted. At that time the patient was placed on treatment with 250 mg. of aureomycin daily for 21 days (21 Gm.). No visible changes were noted.

Case 2.—J. V., aged 64, was first seen by us in May 1949 for a painless enlargement of the left side of his nose, which had been noted eight or nine months previously. History revealed the fact that he first noticed the appearance of tumors on his nose in 1945 and had been seen on several occasions in the Department of Dermatology and Syphilology of the Louisville General Hospital, where a diagnosis of rhinophyma and atypical cysts had been made. Treatment had consisted in electrodesiccation of several of the nodules, and, although biopsy was planned and recommended, the patient did not return to the clinic until nearly two years later. At this time 200 r, unfiltered, was administered, in divided doses, to two infiltrated nodules. These regressed rapidly. Numerous recurrences were noted, and in February 1949 a biopsy specimen was taken and the lesions again electrodesiccated. The pathological report, by Dr. A. J. Miller, was that the condition was lymphoma cutis, type undetermined. Numerous lymphocytes and reticulum cells were noted.

The past history was irrelevant, except that the patient had frequented the General Hospital for many minor ailments, at which times blood counts, all of which were essentially normal, had been made. Repeated blood Kahn examinations likewise gave negative reactions.

Examination and Clinical Course.—When first observed by us the patient presented a definite swelling evenly distributed over the upper two thirds of the left side of the nose. In the upper portion, a deep nodule, which was about 6 or 7 mm. in diameter, was felt. The entire mass had a cystic feel, and the overlying skin was studded with fine telangiectatic vessels. Scars from previous removals of lesions were noted. No clinical signs of rosacea were observed. A few nondescript, 1.5 cm. in diameter erythematous macules were noted in the left temporal area, in front of the left ear and about the left side of the mandible but at the time were felt to be of no significance.

A biopsy specimen taken at the time of the original visit was too small for proper study and interpretation.

Laboratory Data.—A blood Kahn test gave a negative reaction. Repeated hematological studies, including examination of the bone marrow, by Dr. Marion F. Beard, showed an essentially normal condition. A typical blood count was that of June 1949, which was as follows: total white blood cells, 6,900; total red blood cells, 4,400,000; hemoglobin, 14.5 Gm. (94.1 per cent); polymorphonuclear leukocytes, 75 per cent; nonsegmented cells, 5 per cent; lymphocytes, 21 per cent; monocytes, 1 per cent, and color index, 1.09, with slight anisocytosis.

15. The aureomycin used in this study was furnished by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Histopathologic Picture.—After reviewing the original histological section on the patient (which was loaned to us by Dr. A. J. Miller, pathologist, University of Louisville School of Medicine) and correlating the clinical and hematological observations, we felt that this patient had a diffuse type of lymphocytoma cutis. Since Dr. Harry Weeter was familiar with case 1, we asked his opinion in this case. His report was as follows: "The tumor proper was composed of a fairly solid mass of small lymphocytes, characterized by irregularity in the size and staining reaction of the nuclei. These cells appeared to be mature lymphocytes. Among the smaller lymphocytes were somewhat poorly defined areas of larger cells, with rather pale-staining nuclei. They resembled the germinal center of lymph nodes. Mitotic figures frequently found in the germinal center of normal lymph nodes were lacking. There was a very scanty reticular network. Capillary and small blood vessels were present but did not appear unusual. The tumor consisted of an accumulation of cells of the lymphocytic series of the mature type. I consider the lesion a benign lymphocytoma cutis."

Fig. 6 (case 2).—*A*, note diffuse nodular swelling of nose, with superimposed telangiectatic vessels, and scars from removal of previous nodules. *B*, note gross deformity of nose.

Dr. Hamilton Montgomery likewise examined these sections and concurred in the above diagnosis. It is interesting to note that Dr. Montgomery also examined the first section in case 1, which we felt was unsatisfactory for diagnosis, as well as a similar, though unsatisfactory, section from this patient's nose. He felt that the infiltrate was similar in both and that both represented cases of lymphocytoma cutis.

Drs. Stephan Epstein and John B. Miale also examined these sections. Dr. Miale felt that all three sections from the recent biopsy specimens were more or less similar and that they resembled the original biopsy specimen taken from the nose. He reported, "Both were characterized by heavy lymphocytic infiltration, occasionally nodular in the corium. The picture is certainly to be differentiated from lymphoblastoma, especially some of the slides from the recent biopsy specimens (face and ear), in which cellular infiltration appeared diffuse with no nodular formation. I feel, however, that these specimens fit better with the diagnosis of lymphocytoma." Dr. Epstein concurred in the above opinion but emphasized the correlation of the clinical observations with the histological. In one section we felt there was a definite germinal center present. There was some question as to the accuracy of this observation, however, for Dr.

Hamilton Montgomery was inclined to think the picture might have been that of a hair follicle cut on the bias. Without serial sections one could not rule out this possibility. Epstein has repeatedly emphasized that long and tedious search of many sections from several lesions may be necessary before a typical germinal center is found.

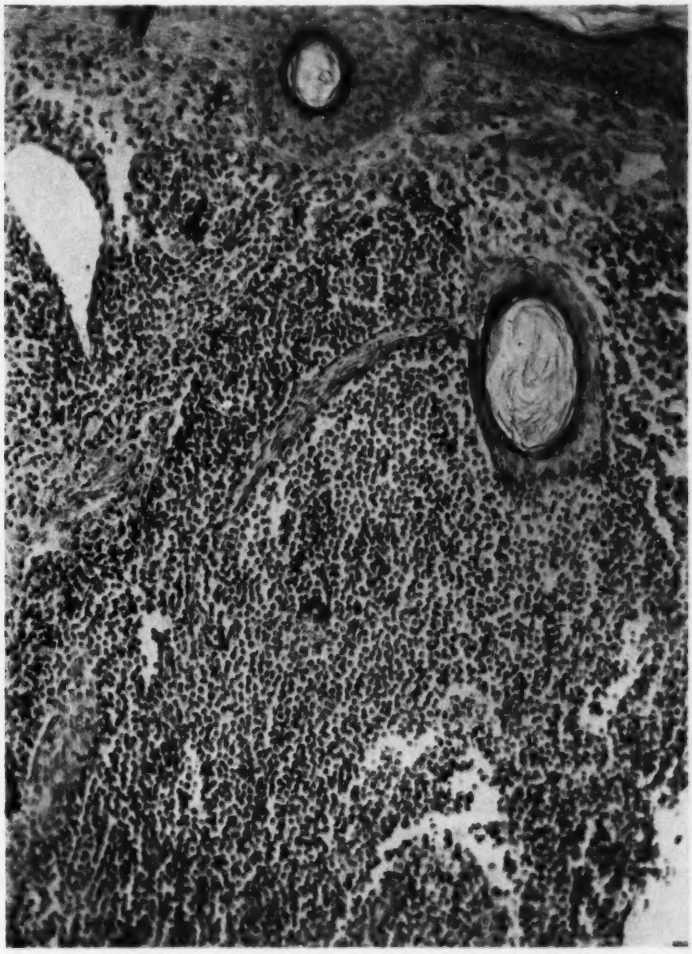

Fig. 7 (case 2).—Low power view of section. Note intermingling of small lymphocytes and larger cells with pale nuclei. The infiltrate is diffuse, with no tendency to form nodules or germinal-center-like areas.

Therapy.—This patient was treated much the same as the patient in case 1, except that no antibiotics were employed. The response to roentgen irradiation was equally satisfactory. In December 1949 the patient returned, complaining of lesions on the left side of the face and ear. Examination revealed nodules in the left temporal area, in the region of the left side of the mandible and the left ear lobe, arranged in a rather atypical zosteriform distribution. On

the anterior aspect of the left ear lobe there was a semitransparent, pearly, almost normal skin-colored nodule 7 mm. in diameter which was rather elastic to palpation and suggestively herpetiform in arrangement of the individual papular elements. On the posterior part of the lobe was a 7 to 8 mm. round nodule, which, however, was not as herpetiform. Undoubtedly several of these nodules had arisen from some of the nondescript macular lesions originally noted, to which no significance had been attached. It is interesting to note that although the arsenic preparation previously administered may have delayed development of the nodules it did not cause their disappearance. Administration of 150 r, unfiltered, repeated three times, at three week intervals, brought about complete resolution of the lesions. In fact, by one week after the original roentgen ray treatment they had practically disappeared. When the patient was last seen, in June 1950, no active cutaneous lesions were noted.

Three biopsy specimens taken, two from the ear lobe and one from the lesion about the mandible, were essentially similar and presented practically the same histological characteristics as the original section taken from the nose.

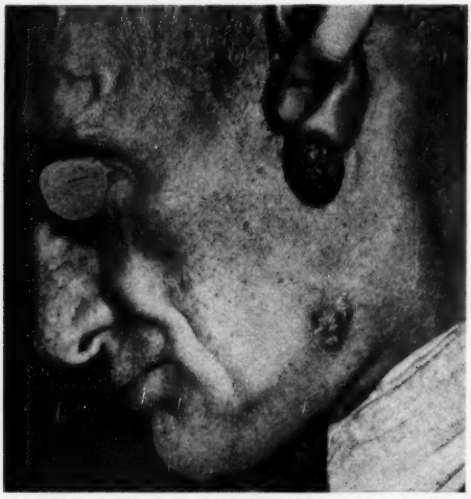

Fig. 8 (case 2).—Typical nodule on ear lobe. Also note nodules in front of ear and about mandible. Previous nodular swelling of nose has completely disappeared.

CASE 3.—A third case, believed to be of lymphocytoma cutis, was recently seen, but it is not included in this series because follow-up examinations and further studies after the initial visit were not possible.

The case was that of a 68 year old woman who presented subcutaneous plaquelike nodules, of at least four years' duration, on the right side of the face. The clinical picture was very similar to that of the so-called plaque type of Spiegler-Fendt sarcoid. A blood count was essentially normal, and physical examination revealed no evidence suggestive of any of the malignant lymphoblastomas.

A biopsy showed what we felt to be a diffuse type of lymphocytoma cutis, although a general pathologist reported the lesion as a growth of low grade malignancy of the lymphoblastoma group.

COMMENTS

Clinical Diagnosis.—Although lymphocytoma cutis is uncommon, there is no doubt that it is a clinical entity which has been frequently overlooked because of its similarity to or confusion with other, commoner conditions. The clinical appear-

ance may differ considerably, as is obvious from the two cases reported herewith. The lesions in case 1 were quite similar to epithelioma adenoides cysticum. Such similarity was likewise noted in the cases of Hallam and Vickers [6] and of Hellier.[7] Our second case and the case of Hellier [7] were strongly suggestive of rhinophyma, but in neither instance was there clinical evidence of a rosacea diathesis or present or past evidence of active rosacea. The diffuse swelling with the localized subcutaneous mass felt on palpation brought to mind a sebaceous cyst, but the failure to evacuate any cystic material plus the fact that the overlying skin was not fixed to the underlying structure seemed to rule out that possibility. When this patient manifested the zosteriform nodules on the face, particularly with involvement of the ear lobe, the clinical diagnosis became much more evident. Involvement of the ear lobes is very common in lymphocytoma cutis. Both of our cases showed this localization, and case 2 was practically identical in appearance to one reported by Bäfverstedt.[8] Any differential diagnosis of lymphocytoma cutis should include lupus miliaris disseminatus, the localized type of Spiegler-Fendt sarcoid, the small papules of neurofibromatosis, miliary sarcoid (Boeck), keloid, malignant lymphoblastoma, lymphangioma circumscriptum and particularly benign cystic epitheliomas. Undoubtedly, as more cases are recognized and reported, there will be listed an even greater diversity of cutaneous conditions from which this entity is to be differentiated.

For a more comprehensive discussion of diagnosis and classification as to clinical types the reader is referred to the monograph by Epstein.[5] According to Bäfverstedt [8] there are two distinct forms—the localized type, consisting of either an isolated lesion or several regionally localized tumors, and the multiple disseminated tumefactions. The former are the commoner, and both of our cases belong to this type. Bäfverstedt believes that the localized form may attack children and adults alike whereas the disseminated type is usually found in adults. The prognosis for life is excellent, since the disease is benign. Malignant degeneration, according to Bäfverstedt,[8] has never occurred.

Histopathologic Picture.—There are few, if any, epidermal changes noted in lymphocytoma cutis, and when present they are of secondary importance. The subepidermal zone is frequently free from any infiltration. Beneath this zone, however, there is an infiltration of cells, occasionally only mature lymphocytes but usually consisting of small, deep-staining lymphocytes and larger reticulum cells with pale nuclei. Not infrequently the infiltrate is supported by a fine reticulum. The architectural arrangement may differ in that the infiltration may be of two distinct types—namely, circumscribed, or nodular, and diffuse—either of which may or may not show true germinal centers or germinal-like areas. This point has been emphasized previously by both Epstein [11] and Montgomery.[11] If the germinal center is present and is surrounded by a capsule, as in some of Epstein's cases, then the histological picture is practically pathognomonic, although Allen [16] has recently ascribed a similar histological picture to the bites of arthropods. However, pronounced epidermal changes which do not occur in lymphocytoma cutis were noted in such cases. Mitoses may occasionally be noted but are not a prominent feature in the pathological picture. In the early lesions with less diffuse infiltration the cells are not infrequently perivascular and surround the

16. Allen, A. C.: Persistent Insect Bites, Am. J. Path. **24**:367, 1948.

hair follicles and glands. If the infiltrate is extensive the normal skin appendages are not seen.

In spite of the histological characteristics of lymphocytoma cutis it is impossible at times to distinguish the diffuse type of infiltrate without germinal centers from the picture of malignant lymphoblastomas, particularly lymphosarcoma and leukemia. According to both Montgomery [14] and Bäfverstedt [8] the histological changes seen in the lymph nodes in follicular lymphoma are quite similar to those of lymphocytoma cutis. In fact, Lever [17] groups localized Spiegler-Fendt sarcoid and lymphocytoma cutis under the heading of follicular lymphoma. We have reviewed the work of Lewis [18] and feel that perhaps some of his cases of Spiegler-Fendt sarcoid might better be grouped with lymphocytoma cutis. The clinical description of the cases, as well as certain histological features, is quite similar. Likewise both conditions respond satisfactorily to roentgen irradiation and arsenical therapy. Regardless of whether or not these two conditions are identical, they have much in common, and until more is known about them they should be grouped together.

Since the clinical picture and the histological observation differ in certain cases, how, then, can one establish a definite diagnosis? It is felt that a final diagnosis can be confirmed only by correlation of the clinical and histological observations along with repeatedly normal observations on hematological and bone marrow studies. It is assumed first that there exists a high index of suspicion. The differentiation from a leukemic infiltration of the skin is of the utmost importance, and, while the resemblance between the two conditions is striking, both clinically and histologically, the differentiation can and must be made by (1) the absence of other evidence of leukemia in blood and bone marrow studies, as well as the absence of observations suggestive of leukemia on general physical examination, and (2) the progress of the patient over a period of years. This last point is most important, and periodic follow-up examinations are imperative. In our two cases we feel that this follow-up period of observation has been and is being satisfactorily maintained.

Nomenclature and Etiology.—In addition to the term lymphocytoma cutis, this condition has been referred to under various names, such as "benign lymphadenoid granuloma of the skin," "miliary lymphocytoma," "lymphadenosis" and "lymphadenosis benigna cutis" (Bäfverstedt).

Lewis [18] was the first to emphasize the importance of dividing the classification of Spiegler-Fendt sarcoid into localized and disseminate types, and, although he did not propose an entirely new terminology, he felt that neither was related to true sarcoid, as that disease is now known, and that the two types were different. Bäfverstedt [8] is of the opinion that certain cases of what has been known as Spiegler-Fendt sarcoid are identical with lymphocytoma cutis. We are of the same opinion.

The etiology of lymphocytoma cutis is unknown. Since there is a predilection for exposed areas of the body, it is felt by some that light sensitivity plays a part. This may have been a contributing factor in our first case. Still others feel that some trauma, such as insect bites, is responsible. Bäfverstedt [8] feels that the

17. Lever, W. F.: Histopathology of the Skin, Philadelphia, J. B. Lippincott Company, 1949, p. 420.

18. Lewis, G. M.: Is Spiegler-Fendt Sarcoid a Clinical or Histologic Entity? Arch. Dermat. & Syph. **31**:67 (Jan.) 1935.

condition may be caused by various stimuli, such as trauma, toxins or even venous stasis.

Therapy.—Of the various types of treatment that have been suggested, we feel that the most efficient is roentgen irradiation. Mopper and Rogin [12] are of the same opinion. In fact, the response to roentgen irradiation is so striking that one might say that if the local lesions do not disappear completely or show pronounced regression after 300 to 400 r the diagnosis should be questioned. Penicillin and aureomycin were administered in one of our cases, with no demonstrable effect on the lesions. Although in both of our cases roentgen radiation and an arsenical were given concomitantly, the regression of the lesions was too rapid to attribute to arsenical therapy. Furthermore, the arsenic preparation did not cause the disappearance of the early lesions noted in case 2. Bäfverstedt likewise attributes his therapeutic successes to roentgen ray therapy alone. Even though there was a good response to superficial roentgen ray therapy, the lesions frequently recurred. This recurrence took place regardless of the therapeutic modality employed.

SUMMARY AND CONCLUSIONS

Two cases of localized, multiple type lymphocytoma cutis are reported and the literature briefly reviewed.

The clinical differential diagnosis and histological characteristics are discussed, and the necessity of the existence of a high index of suspicion before differential diagnosis is emphasized.

An accurate diagnosis can be confirmed only by correlation of the clinical and histological observations along with repeatedly negative results of hematological and bone marrow studies.

The necessity for observation for many years to rule out the malignant lymphoblastomas is stressed.

The clinical and histological similarity of certain localized types of Spiegler-Fendt sarcoid and lymphocytoma cutis is emphasized.

The lesions of lymphocytoma cutis are extremely radiosensitive.

In the cases herewith reported, regardless of the type of therapy employed, local recurrences in scar tissue and new lesions were frequently encountered.

Dr. Stephan Epstein, of the Marshfield Clinic, Marshfield, Wis., and Dr. Hamilton Montgomery, of the Mayo Clinic, Rochester, Minn., gave help in the preparation of this paper.

ABSTRACT OF DISCUSSION

Dr. Samuel Becker, Chicago: Lymphocytoma cutis is rare in my experience. Drs. Loveman and Fliegelman are fortunate in having had two patients with the disorder in so short a period. My own experience consists of study of only a few cases. At the University of Chicago Dermatological Laboratory we have about 2,000 specimens a year, and over a period of some 22 years we have seen only a few instances of this disorder. There may, of course, be patients who have been treated without biopsy and in whom the condition was not observed by us.

One of our patients was a middle-aged woman who had a semiglobular, slightly translucent tumor on the cheek. Dr. Loveman did not mention the diascopic feature, which I think is diagnostic. Diascopic pressure shows the same apple color as that seen in tuberculosis. That observation may be one reason why the name sarcoid was given to the condition by Spiegler and Fendt.

A biopsy was made of the lesion, and a solid infiltration of mature lymphocytes was evident. The entire tumor was excised with a certain amount of normal skin, but after a few months there

was recurrence at one pole of the scar. Dr. Loveman has also emphasized this great tendency for recurrence.

Cognizant of the rarity of reports of such a disorder, I was desirous of reporting this case but was deterred by a query from Dr. P. E. Delaney, a general pathologist, who regularly attended our histopathological seminars: "How do you know that the tumor is not a lymphocytic tubercle?" Of necessity, my answer was, "I do not know." That fact deterred me from reporting the case as lymphocytoma.

I believe that persistent insect bites can be differentiated by inflammatory changes with eosinophilic leukocytes. Lymphosarcoma is distinguished by the presence of many mitotic figures. Leukemia cutis is distinguished by blood studies and by hepatic, splenic and sternal biopsies. Spiegler-Fendt sarcoid may be identical with lymphocytoma cutis. Further studies carried out in the same careful way as that used by Drs. Loveman and Fliegelman will be necessary to clarify this still somewhat confused group of disorders.

Dr. George C. Andrews, New York: Like Dr. Becker, I have seen two cases of this disorder throughout the years. It is very rare. I believe it is a real entity. I suspect, though, that it would be better to confine the diagnosis to cases of idiopathic origin—without history of exposure to sunlight, without insect bites, without any obvious cause, without reaction to outside influences. I suspect that probably the lymphocytic tubercle or some analog of that sort may be the explanation of the real cases of this disease. Usually the lesions, if multiple, are grouped; they occur mostly on the face, with a tendency to affect the nose and the ears, and they do respond very quickly to roentgen ray treatment.

I have seen mistakes made in this diagnosis. Some insect bites, with their reactions, look exactly like this. Also, my associates and I have in our care now a patient who is an art designer. who, every time he goes out in the sunlight and gets a lot of sunlight, acquires lumps in his skin. He will acquire 25 or 30 lumps after exposure to the sunlight over a week end on his yacht, and these lumps will last for several days and itch intensively. Histologically they look like lymphosarcoma or lymphocytoma, more like one than the other. This process goes on and on.

I have also seen a mistake made in giving a lesion the diagnosis of lymphocytoma cutis when it was an anaplastic epithelioma. We must be very careful in diagnosing these cases; we must watch them carefully, and, if they do not respond rapidly to roentgen ray treatment, we should possibly take another biopsy specimen, because further study may show an anaplastic epithelioma.

Dr. Lawrence C. Goldberg, Cincinnati: I should like to add a historical note to this particular paper. It was new to me that Dr. Jadassohn had described this disorder in 1906. The first case that my associates and I had recalled was of a patient we saw at the International Congress in 1935, at which time Berry described the case; I had the privilege of making the rounds at that time with Dr. Fred Wise, and he stated that he had not seen any cases up to that time. I believe it probably is a new entity as far as the Americans are concerned, probably an old one as far as the Europeans are concerned.

Dr. W. B. Guy, Pittsburgh: I believe I have seen one case of this entity. It was in a white woman, in her fifties. She had multiple nodules on her ears, arms, forearms and hands. Biopsy showed them to be composed entirely of lymphocytes. Her white blood cell count was slightly higher than normal, with a slight predominance of lymphocytes. We thought she had chronic lymphatic leukemia with leukemia cutis.

We told the patient's family that the eventual outlook was grave and hospitalized her for a course of nitrogen mustard therapy. With this treatment the nodules flattened quickly and the white blood cell count came down a bit. That was two years ago, and the patient is still alive and well. There have been occasional recurrences of some of the lesions, and these have responded to roentgen ray therapy.

I believe that this patient had lymphocytoma cutis instead of leukemia and suggest nitrogen mustard as another form of therapy for it, particularly when the lesions are widespread.

Dr. Harry L. Arnold, Honolulu, T. H.: I should like to ask Dr. Loveman, apropos of his statement that these lesions do not eventuate in malignant growth, whether he feels the presence of well developed germinal centers has any bearing on this question. My associates and I had a patient in 1941, a middle-aged woman with a group of four brownish translucent nodules in the middle of her forehead. They had been excised before I had an opportunity to see them. They

turned out to be lymph follicles with very well developed germinal centers. The patient was merely observed because it was felt that the lesion had been completely excised.

Four months later, three new nodules, which were said by the surgeon to be identical with the original ones, appeared in the scar. These were excised; two resembled the previous nodules, and one showed well developed infiltration of lymphosarcoma. Dr. Paul Klemperer reviewed the section and concurred in the diagnosis.

Dr. George M. Lewis, New York: From the evidence given by the authors, it would seem that the disease under discussion is identical with the localized form of Spiegler-Fendt sarcoid, with which all dermatologists are familiar. I wish to caution those who believe that this disorder may always be benign. In spite of the good prognosis which one may expect in most instances, there is an occasional patient in whom the localized form of the disorder, with a solitary or limited number of lesions, is controlled for a number of months with roentgen rays but in whom the final outcome is generalized lymphosarcoma. We should regard these cases with just a little caution and not consider the prognosis altogether banal.

Dr. A. B. Loveman, Louisville, Ky.: It is always a source of real satisfaction when anyone discusses my paper, and I wish to thank each and every one of you. I now should like to take up some of the various points in detail.

Dr. Becker's suggestion of employing diascopy as a diagnostic aid is definitely worth while, and in the future we shall certainly carry out this procedure. Incidentally, in the full length manuscript there is a third case.

I feel that Dr. Becker should not be perturbed by what the general pathologist says about malignant lymphoblastoma, because several pathologists made a diagnosis of malignant lymphoblastoma in our cases. One of them finally agreed with our diagnosis of lymphocytoma cutis, but in study of a later section from the same patient he apparently had forgotten this conclusion and again diagnosed the condition as a malignant growth.

Concerning Dr. Andrews' remarks, I should like to state that we are familiar with his two cases and have quoted him extensively in the original paper. We are also aware of the pathological changes similar to lymphocytoma cutis which result from insect bites. This condition has been stressed by Allen.

I should like to state that Jadassohn was credited with reporting the first case but reported it as a pseudoleukemic infiltration of the skin. This was subsequently classified as a case of lymphocytoma cutis.

I appreciate Dr. Guy's remarks concerning nitrogen mustard, and, if the occasion arises, we shall certainly use it.

With regard to Dr. Arnold's question as to whether or not the prognosis is better in the localized type, I should like to say that, provided that the diagnosis is correct, I see no reason why the prognosis in the two types should not be the same. The diffuse type, however, is frequently confused with one of the lymphoblastomas, and thus our prognosis in such cases should perhaps be somewhat guarded.

BENIGN SOLITARY LYMPHOCYTOMA

Report of Three Cases

COLEMAN MOPPER, M.D.
AND
JAMES R. ROGIN, M.D.
DETROIT

ALTHOUGH benign lymphocytomas have been described in the literature since 1906 and approximately 56 cases are reported, there is still some doubt expressed in textbooks of dermatology as to the exact classification of this non-malignant lymphocytic growth. Sutton and Sutton [1] stated that they were hesitant to admit the existence of a wholly benign adult lymphocytoma. Ormsby and Montgomery [2] in their brief discussion stated that "dermatologists, under the title of lymphocytoma of the skin, have described miliary nodules, especially on the face, but also occurring on the scrotum and extremities, which simulated clinically a miliary sarcoid or lupus miliaris disseminatus." Further, they stated that there are no hemocytological changes and that the similarity of the histological changes to those seen in the more benign types of follicular lymphoblastomas would suggest a close relationship between the two conditions. Andrews [3] described both solitary and miliary lymphocytomas.

Jadassohn,[4] in 1906, presented a case of a 33 year old woman who had small semitranslucent nodules on both cheeks. These had been present since 1892. The patient was in excellent health at the time of his presentation. Jadassohn diagnosed this case as a pseudoleukemic infiltration of the skin, noted that the histological structure of the tumors was most unusual and stated that the patient would be followed closely to see whether or not leukemic changes developed. Biberstein,[5] in 1922, demonstrated a case at Breslau, and, in discussing this case, Jadassohn commented that his original patient had never manifested any signs of leukemia and that her skin tumors had remained unchanged. Kauffmann-Wolf,[6] in 1921,

From the Department of Dermatology and Syphilology, Dr. Loren W. Shaffer, professor, Wayne University Medical School, Detroit.

1. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

2. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948.

3. Andrews, G. C.: Diseases of the Skin, ed. 3, Philadelphia, W. B. Saunders Company, 1946.

4. Jadassohn, J.: Arch. f. Dermat. & Syph. **82**:297, 1907.

5. Biberstein, H.: Lymphocytome, Zentralb. f. Haut- u. Geschlechtskr. **6**:70, 1923.

6. Kauffmann-Wolf, M.: Scrotal Lymphocytoma of Children, Arch. f. Dermat. u. Syph. **130**:425, 1921.

presented two children who had nodules on each side of the median raphe of the scrotum, which showed lymphocytic tissue. She was the first to use the term "lymphocytoma," because of the very close resemblance that the large majority of the cells have to lymphocytes. Histologically, Jadassohn [4] noted that his case showed, almost exclusively, lymphocytes arranged in a fine reticulum, with some areas arranged in follicles, but here and there were a few plasma and giant cells. Carol and Prakken,[7] in 1939, stated that about 50 cases had been recorded, all the cases being in the European literature. Since then, several cases have been described in the American literature by Wise,[8] MacKee,[9] Netherton,[10] Lentz and Beerman,[11] Andrews,[12] Epstein,[13] Foerster [14] and, undoubtedly, others. Bäfverstedt,[15] in 1943, presented an extensive report of a group of tumors of the cutis and subcutis composed of lymphoreticular tissue and characterized by a benign course, but, for the most part, they fell into the Spiegler-Fendt sarcoid group, although others he designated as lymphocytomas. He suggested the term lymphadenosis benigna cutis and mentioned that malignant degeneration does not occur in lymphocytomas.

Lymphocytomas occur in both sexes but are observed more frequently in women. The youngest patient was 4 years old (Kauffmann-Wolf's case), and the oldest was Freund's patient, 75 years old. Clinically, two forms are recognized, according to Bäfverstedt [15]: (1) those characterized by a solitary lesion or several localized tumors in a small area and (2) those characterized by multiple, disseminated tumors.

Epstein,[16] in 1935, gave a more elaborate classification: (1) lymphocytoma miliare faciei, this group including the great majority of cases described; (2) lymphocytoma tumidum, a heading which includes the lymphadenoid tumors located particularly about the pinna; (3) lymphocytoma genitale of the scrotum; (4) lymphocytoma genitale of the labia majora, and (5) lymphocytoma miliare faciei of the disseminated type.

Whether the lesions are of the solitary type or the multiple type, the general health of the patient is unaffected and there is no enlargement of the spleen or

7. Carol, W. L., and Prakken, J. R.: Lymphocytoma, Acta dermat.-venerol. **20**:147 (March) 1939.

8. (*a*) Wise, F.: Disseminated Miliary Lymphocytoma of Face and Neck, Arch. Dermat. & Syph. **39**:749 (April) 1939; (*b*) Localized Lymphocytoma, ibid. **46**:170 (July) 1942.

9. MacKee, G. M.: Lymphocytoma of Nose, Arch. Dermat. & Syph. **50**:141 (Aug.) 1944.

10. Netherton, E. W.: Aleukemic Lymphocytosis Cutis (Lymphocytoma of Skin), Arch. Dermat. & Syph. **57**:779 (April) 1948.

11. Lentz, J. W., and Beerman, H.: Lymphocytoma Cutis, Arch. Dermat. & Syph. **60**: 459 (Sept.) 1949.

12. Andrews, G. C.: Lymphocytoma, Arch. Dermat. & Syph. **60**:1011 (Nov.) 1949.

13. Epstein, S.: Lymphocytoma Miliare Faciei: Case Report, Arch. Dermat. & Syph. **59**:365 (March) 1949.

14. Foerster, O. H.; Foerster, H. R., and Ruch, D. M.: Lymphocytoma: Case Report, Arch. Dermat. & Syph. **60**:874 (Nov.) 1949.

15. Bäfverstedt, B.: Lymphocytoma: Clinical and Anatomicopathologic Study, Acta. dermat.-venerol. (supp. 11) **24**:1, 1943. Sulzberger, M. B.: 1945 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1946.

16. Epstein, S.: Lymphocytoma of Skin with Involvement of Bulbar Conjunctiva, Arch. f. Dermat. u. Syph. **173**:181, 1935.

lymph glands. The blood picture is within normal limits, although a few cases have shown a slight lymphocytosis. The etiology of this disorder is unknown, and whether the lesions are inflammatory, follow trauma or are neoplastic still occasions discussion. Epstein [16] described two cases in which the patients were heliosensitive, and he therefore thought that the chronic irritation of a solar dermatitis had initiated these lymphocytic tumors.

Hellier [17] found a definite history of injury to the affected part (nose) prior to the onset of tumor development. Hallam and Vickers [18] stated that "In all proved cases described, the onset of leukemia has never been reported." Emphasis has been given by several authors, including Epstein, to the necessity of accurate diagnosis of these lesions and of keeping them under rigid observation for possible future lymphoblastomatous changes.

Lewis [19] was the first to emphasize the differentiation between the localized and disseminate types of Spiegler-Fendt sarcoid, although he wisely did not confuse the issue with new terminology. Bäfverstedt [15] was of this same opinion. Loveman and Fliegelman [20] were of the opinion that some of Lewis' cases of Spiegler-Fendt sarcoid should be classified with lymphocytoma cutis and, in their conclusions, stated that "The clinical and histological similarity of certain localized types of Spiegler-Fendt sarcoid and lymphocytoma cutis is emphasized." Lewis, in commenting on the cases of Spiegler-Fendt sarcoid, said, "All the histologic evidence fitted in with the lymphoblastomas or lymphocytomas but was somewhat different from the diseases described under this heading." We feel that the first three cases reported by Lewis were compatible with lymphocytoma, but the fourth case was probably a lymphosarcoma. Montgomery [21] stated that "so-called Spiegler-Fendt sarcoid and some, if not all, follicular lymphoblastomas (giant follicle lymphomas), and most cutaneous lymphocytomas, represent variants of reticulum-cell and lymphocytic types of lymphosarcoma." In the same discussion, Montgomery further stated that "Lymphosarcoma may have a primary autochthonous cutaneous origin and may run a relatively benign course, as is true also of certain types of Spiegler-Fendt sarcoid, cutaneous lymphocytoma and follicular lymphoblastomas."

Montgomery,[22] Epstein [16] and Loveman and Fliegelman,[20] were all in agreement that, histologically, there are two types of lymphocytoma, the diffuse and the circumscribed or nodular. Typical germinal centers need not be present for the diagnosis to be made, but Loveman and Fliegelman [20] felt that if germinal centers are present and are surrounded by a capsule, the histological picture is almost pathognomonic. It was Loveman and Fliegelman's further opinion that "In spite

17. Hellier, F. F.: Lymphocytoma of Face, Brit. J. Dermat. **51**:260 (June) 1939.

18. Hallam, R., and Vickers, H. R.: Two Cases of Miliary Lymphocytoma or Benign Lymphadenoid Granuloma of Skin, Brit. J. Dermat. **51**:251 (June) 1939.

19. Lewis, G. M.: Is Spiegler-Fendt Sarcoid a Clinical or Histological Entity? Arch. Dermat. & Syph. **31**:67 (Jan.) 1935.

20. Loveman, A. B., and Fliegelman, M. T.: Lymphocytoma Cutis: Report of 2 Cases, Arch. Dermat. & Syph., this issue.

21. Montgomery, H.: Mycosis Fungoides, Lymphoblastoma of the Skin and Allied Conditions as General Diseases, in Oxford Loose-Leaf Medicine, to be published.

22. Montgomery, H.: Personal communication to the authors.

of the histological characteristics of lymphocytoma cutis it is impossible at times to distinguish the diffuse type of infiltrate without germinal centers from the picture of malignant lymphoblastomas, particularly lymphosarcoma and leukemia."

REPORT OF CASES

Two of the cases presented herewith exhibited solitary lesions, and the third case, which exhibited one large lesion, with an attached satellite smaller lesion, even in the broadest interpretation could not be classified as multiple or disseminated. In all three cases the lesions were found on the face only.

CASE 1.—J. R., a Russian white man aged 44, was first seen by us on Feb. 15, 1945. He stated that about six weeks previously a small lesion had appeared on the left side of the nose and that it had been enlarging gradually since its onset.

Examination.—There was a tumor on the left side of the nose just above the outer aspect of the left nostril and extending down to the left nasolabial fold. The lesion was oval, the short diameter being from above downward. The tumor was approximately 1.5 cm. in diameter, the long diameter being 2 cm. It was slightly elevated, about 0.25 cm. above the level of the surrounding normal skin. The surface was convex in all directions. The tumor was dull brownish to purplish and was doughy to spongy or elastic. It was not tender to pressure or painful in any way.

White blood cell counts taken initially and 10 months later were 6,500 and 5,700, respectively. Differential studies of the smear were normal on both occasions and showed 20 to 26 per cent lymphocytes.

A biopsy specimen was taken from the center of the lesion and reported by Dr. Hermann Pinkus as follows: "The epidermis and uppermost portions of the corium were normal. The deeper parts were very densely infiltrated with lymphocytes of relatively large size. In between there were small groups of larger cells of reticulum type, some of them multinucleated. There were also large, comedo-like hair follicles and nests of epithelial cells, probably resulting from choking off and destruction of other follicles and sweat glands.

"I should like to call this lesion a lymphoma and do not believe that it has the malignant implications of lymphoblastoma. However, as the biopsy specimen was taken from the center of the lesion, it is impossible to know what the borders look like from it. In order to call the lesion a lymphocytoma, I should like to see germinal centers, which were not present in these sections."

Hamilton Montgomery, in a personal communication on March 17, 1950, stated, "Dr. Stephan Epstein and I have seen cases at the meetings of the Chicago Dermatological Society which both he and I regard as fitting in with lymphocytoma and presenting multiple lesions on the face which histologically failed to reveal germinal centers. I do not believe that germinal centers are necessary for the establishment of the diagnosis of lymphocytoma."

Dr. Montgomery examined the sections Feb. 27, 1945, and reported as follows: "I think the picture in this section would fit in well with a so-called lymphocytoma, or, less likely, with a follicular lymphoblastoma. I am not clear myself just where to place lymphocytoma in relation to lymphoblastoma, although I think they are closely related, and some forms of lymphocytoma do go over into lymphoblastoma."

Clinical Course.—As the lesion was composed primarily of lymphocytes, it was thought that it should prove to be radiosensitive. It was treated, therefore, with roentgen irradiation, a single exposure: 345 r, with 74 kv., 4 ma., and 0.5 mm. Al filtration, through a lead cone to shield the surrounding normal skin.

Ten days later the lesion had involuted about 70 per cent. A repeat dose of 345 r was then given.

Two weeks after the second roentgen treatment the tumor involuted completely, and there was no sign of it except a dull brownish pigmentation, entirely smooth and nonpalpable.

Three and one-half years later there was no sign of the original tumor. The pigmentation noted in 1945 had disappeared completely. The patient had enjoyed completely good health during the five year period since he was first seen by us. Repeated blood studies during this five year period revealed no abnormal hemocytological changes.

CASE 2.—R. M., a white Belgian woman aged 55, was first seen by us Dec. 23, 1947. She stated that her skin lesion had appeared just four weeks previously and had enlarged gradually. There had been no pain, tenderness or history of injury to the involved site.

Examination.—There was an elevated circular erythematous lesion, about 2 cm. in diameter, located in the midglabellar area, between the eyebrows, the lower edge being just above the upper limit of the nose. The elevation was approximately 0.25 cm., and the surface was smooth and slightly convex from above downward and from side to side, producing a semispheric figure from its anterior view. The border of the lesion was well marginated and regular. The tumor mass had a characteristic spongy to doughy or elastic consistency, was not tender and was dull brownish to purplish red. A presumptive diagnosis of lymphocytoma cutis was made, and a biopsy specimen was taken from the lowermost portion of the tumor.

Roentgen irradiation, 150 r, with 0.5 mm. Al filtration, closely shielded through a lead cone, was given. On a return visit, one month later, the lesion had involuted greatly; at that time 250 r, with 0.5 mm. Al filtration, was given. The patient was not seen again for three months, and at that time the tumor had involuted completely and only the biopsy scar marked the site of the original lesion.

The biopsy report by Dr. Hermann Pinkus was as follows: "The sections showed, in agreement with the clinical diagnosis, a lymphoid structure. The entire corium and upper part of the subcutis, with the exception of a narrow strip below the epidermis, was infiltrated densely with mononuclear cells of the small and large lymphocyte type. In between there were quite a few capillaries with prominent endothelia and larger cells of histiocytic type, possibly a few stem cells. There were a few mitoses. There was a scattering of eosinophils around the blood vessels. The normal structure of the corium and most of the appendages were destroyed.

"I like to restrict the term lymphocytoma to a thoroughly benign development of lymphoid tissue in the skin, with well developed germinal centers and no destructive tendencies. I know that others speak of malignant lymphocytomas, but I would prefer to call such growths lymphomas or, if you wish, lymphoblastomas. The terminology is rather confused. I believe it is of some significance that these sections showed destruction of corium and appendages and infiltrating rather than expansive growth. Of course, one cannot predict the clinical course entirely from the histological picture. Granulomatous lesions, such as the infectious granulomas or reticulogranuloma, are destructive but benign. I would designate this lesion a lymphoma, potentially malignant."

Two and one-half years later, this patient was in excellent general health.

CASE 3.—A Negro woman aged 30 was first seen by us in October 1948 and stated that approximately 1.5 cm. in length and 0.75 cm. in width, which was composed of two spherical and since then had enlarged slowly. There was no history of previous injury. The lesion was not tender or painful.

Examination.—On the upper right eyelid there was an elongated, elevated lesion, approximately 1.5 cm. in length and 0.75 cm. in width, which was composed of two spherical lesions, the larger one being twice the size of the smaller. The smaller nodule was actually a part of the larger one and appeared to be an outgrowth from it, the two being joined by a small segment of the edge of each lesion. The entire lesion was elevated 0.5 cm. above the level of the surrounding normal skin. The color of the tumor was the characteristic dusky, brownish, purplish red noted in our two earlier cases. The consistency was doughy to spongy, as in our other cases.

The tumor was excised en bloc at the time of the patient's first visit.

The biopsy report by Dr. Hermann Pinkus was as follows: "There was dense, well circumscribed, tumor-like infiltration of the upper part of the corium. The cells were quite even in size and shape and were mainly lymphocytes. There were a few areas resembling germinal centers. The diagnosis was lymphocytoma."

Fig. 1.—Low power view showing fairly well marginated tumor in case 3.

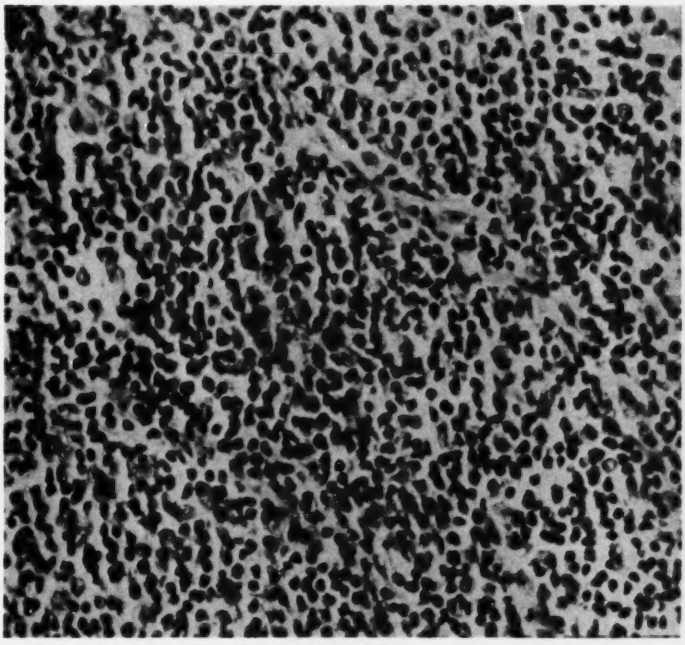

Fig. 2.—High power view showing uniformity of cells in case 3.

COMMENT

It is our opinion that benign lymphocytomas do exist and that these lesions are entirely distinct and separate from highly malignant lymphoblastomas which may involve the skin. The three cases described are best designated as benign solitary lymphocytomas. The differential diagnosis of these solitary tumors is quite lengthy and would include distinction primarily from such entities as sarcoid, eosinophilic granuloma (reticulogranuloma), lupus erythematosus, leukemia cutis, a solitary plaque of benign cystic epithelioma or trichoepithelioma, basal or squamous cell epithelioma, tertiary syphilis, tuberculosis cutis, dermoid cyst, Spiegler-Fendt sarcoid, lymphangioma circumscriptum and sebaceous cyst.

The majority of these lesions seem to occur in women and are located on the face. The sudden onset, rapid growth and lack of cutaneous symptoms, as well as the doughy or elastic consistency, characteristic color and absence of any scaling, are helpful in the diagnosis. These tumors are highly radiosensitive and respond rapidly and spectacularly to small doses of roentgen irradiation.

Another case of suspected lymphocytoma on the nostril was seen by the authors. This tumor disappeared after very small amounts of roentgen irradiation. Since this lesion was not examined microscopically, the case is not included in the series reported herewith. While we advocate biopsy in all suspected cases of lymphocytomas, in order to prove the diagnosis, it is our belief that a presumptive clinical diagnosis can be made in the majority of cases from the characteristic appearance of the lesion. Furthermore, the complete and rapid involution of the lesion following a small dose of roentgen irradiation would add further weight to the presumptive clinical diagnosis.

While fairly high doses of roentgen rays were given in the first case, from our experience in subsequent cases it is believed that much smaller doses would yield the same excellent therapeutic result.

SUMMARY

Three cases of benign solitary lymphocytoma are reported.

These tumors are very sensitive to small doses of roentgen irradiation.

Biopsy is necessary for establishment of an absolute diagnosis; however, the clinical observations and absence of hemocytological changes should, in most cases, strongly suggest the diagnosis.

Benign lymphocytoma is actually lymphocytic proliferation *in situ* and should be distinguished from a localized malignant lymphoblastomatous involvement of the skin.

Malignant degeneration does not occur in benign lymphocytoma.

HYALURONIDASE ACTION IN NORMAL AND IN ROENTGEN-IRRADIATED RABBIT SKIN

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AND
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IN AN INVESTIGATION of the biologic effect of roentgen therapy, hyaluronidase action has been studied in normal and in roentgen-irradiated rabbit skin. Roentgen therapy administered in vitro has been reported as having no effect on hyaluronidase activity.[1] On the other hand, roentgen irradiation may inactivate purified preparation of hyaluronidase.[2] This report concerns a comparative study of the spreading activity of hyaluronidase [3] in normal and in irradiated living tissue.

Hyaluronidase is probably identical with "spreading factor," which was first described by Duran-Reynals [4] in 1929. Meyer [5] pointed out that hyaluronic acid is one of the mucopolysaccharides which act to hold cells together in a jelly-like matrix, to block the spread of foreign matter and to hold water in interstitial spaces. It probably participates in the formation of barriers against infection and in the exchange of water, electrolytes and metabolites. The enzyme hyaluronidase is capable of hydrolyzing or depolymerizing hyaluronic acid and other mucopolysaccharides of the ground substances, thereby reducing the viscosity.

MATERIAL AND METHODS

Twenty-four New Zealand albino rabbits of the same stock and from 12 to 20 weeks of age, weighing from 1.34 to 3.6 Kg., were divided into four groups of six each. These groups are hereinafter referred to as "control" group, "400" group, "800" group and "1600" group. Each group consisted of three males and three females except group "1600," in which there were five females and one male.

From the Department of Dermatology and Syphilology, the Medical College of Alabama.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 20, 1950.

1. Aylward, F. X.: Chemical Nature of the Reynals Spreading Factor from Mammalian Testicle, Proc. Soc. Exper. Biol. & Med. **36**:477 (May) 1937. Duran-Reynals, F.: Tissue Permeability and the Spreading Factors in Infection; A Contribution to the Host : Parasite Problem, Bact. Rev. **6**:197 (Dec.) 1942.

2. Byers, S. O.; Tytell, A. A., and Logan, M. A.: The Production and Some Properties of Clostridium Perfringens Hyaluronidase, Arch. Biochem. **22**:66 (May) 1949.

3. The hyaluronidase used in this investigation was supplied by the Ortho Research Foundation, Raritan, N. J.

4. Duran-Reynals, F.: The Effect of Extracts of Certain Organs from Normal and Immunized Animals on the Infecting Power of Vaccine Virus, J. Exper. Med. **50**:327 (Sept.) 1929.

5. Meyer, K.: The Biological Significance of Hyaluronic Acid and Hyaluronidase, Physiol. Rev. **27**:335 (July) 1947.

Each rabbit was prepared the day before either irradiation or injection by having the fur clipped with electric clippers from both lateral aspects of the trunk, after which procedure a depilatory was applied to remove the remaining hair. The depilatory consisted of barium hydroxide treated with hydrogen sulfide.[6] It removed the hair within three to five minutes and was then washed off with running water. No apparent deleterious effects due to this procedure were noted.

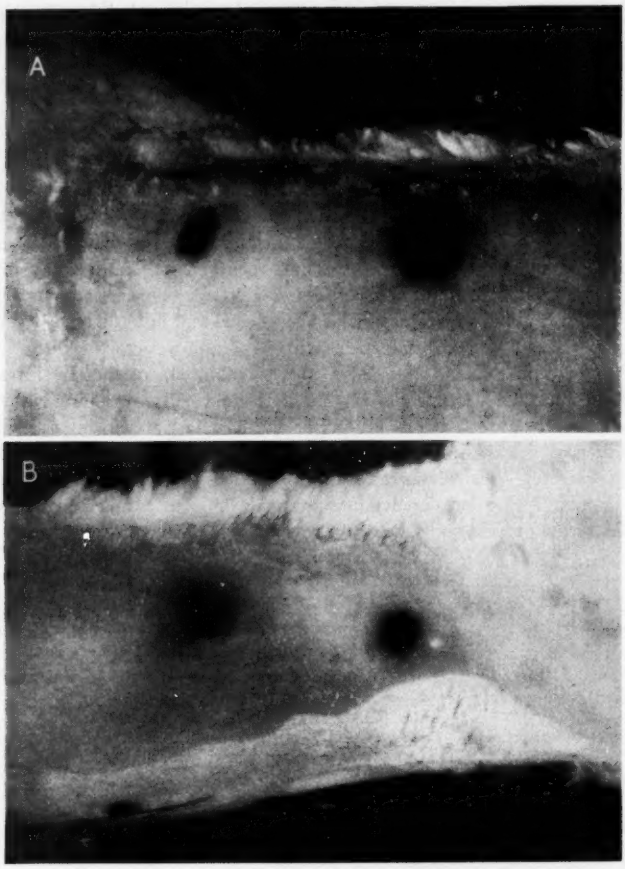

Fig. 1.—*A*, rabbit from "control" group (left flank). This animal received no roentgen ray therapy to either flank. The lesion on the left was photographed 90 minutes after injection intracutaneously of 0.25 cc. of an isotonic solution of sodium chloride plus 0.25 cc. of Higgins india ink. The lesion on the right was also photographed 90 minutes after the injection of the same materials plus 500 turbidity-reducing units of hyaluronidase. *B*, same animal as in *A* (right flank). The lesions were photographed 90 minutes after injection of the same materials as mentioned with regard to *A*. The lesion shown on the left contained hyaluronidase.

6 Carmichael, E. B.: A Convenient Preparation for the Removal of Hair, Science **75**:136 (Jan.) 1932.

Each animal in group "400" received 400 r in a single exposure over the entire left lateral aspect of the trunk from the posterior aspect of the forelimbs to the anterior aspect of the hindlimbs. The head and anterior extremities and the posterior trunk and extremities were covered with 1.0 mm. of lead. This therapy was administered with a Westinghouse dermadex® shock-proof x-ray machine with valve tube rectification. The machine factors for irradiation consisted in 85 kv., 5 ma., no added filtration and a focus-skin distance of 20 cm. with a half-value layer of 0.7 mm. of Al. This machine was calibrated by a certified radiation physicist

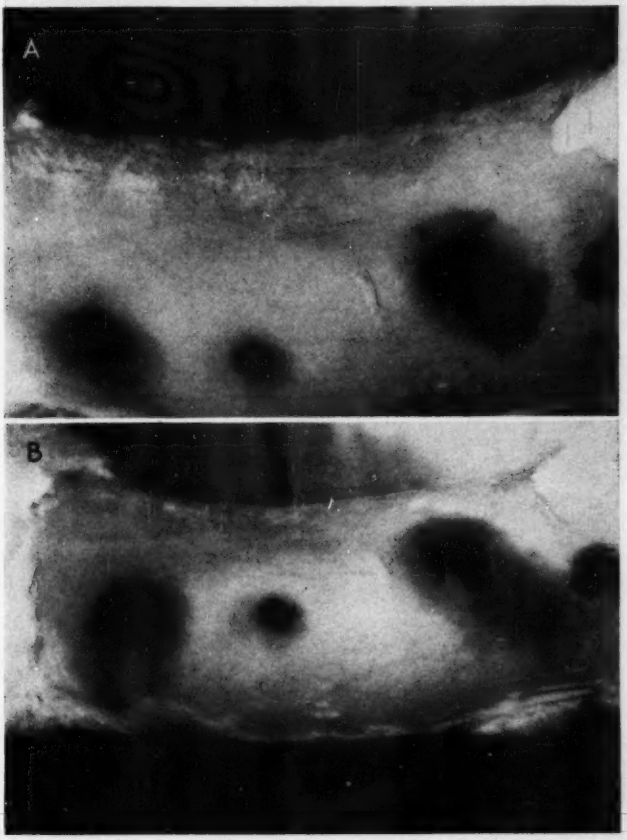

Fig. 2.—*A,* rabbit from "400" group (irradiated left flank). The spreads of the first and second series of injections are shown. The two lesions on the left were photographed five weeks after injection. The two lesions on the right were photographed 90 minutes after injection. In each instance the injection producing the larger lesion contained hyaluronidase. *B,* same animal as in *A* (unirradiated right flank). The two lesions on the left were photographed 90 minutes after injection. The two on the right were photographed five weeks after injection. The larger lesions were produced by injections containing hyaluronidase.

during the investigation. Each animal in group "800" similarly received 800, and in group "1600" each animal received 1,600 r. The control group received no roentgen ray therapy.

One week after irradiation 0.25 cc. of 1 : 2 Higgins india ink (1 part ink, 2 parts isotonic solution of sodium chloride) plus 0.25 cc. of an isotonic solution of sodium chloride was injected

intracutaneously into both sides of each animal in groups "400," "800" and "1600." Simultaneously the same amount of ink plus 0.25 cc. of sodium chloride solution containing 500 turbidity-reducing units of hyaluronidase [7] was injected intracutaneously into both flanks of each animal. The members of the control group at the same time also received two similar injections into

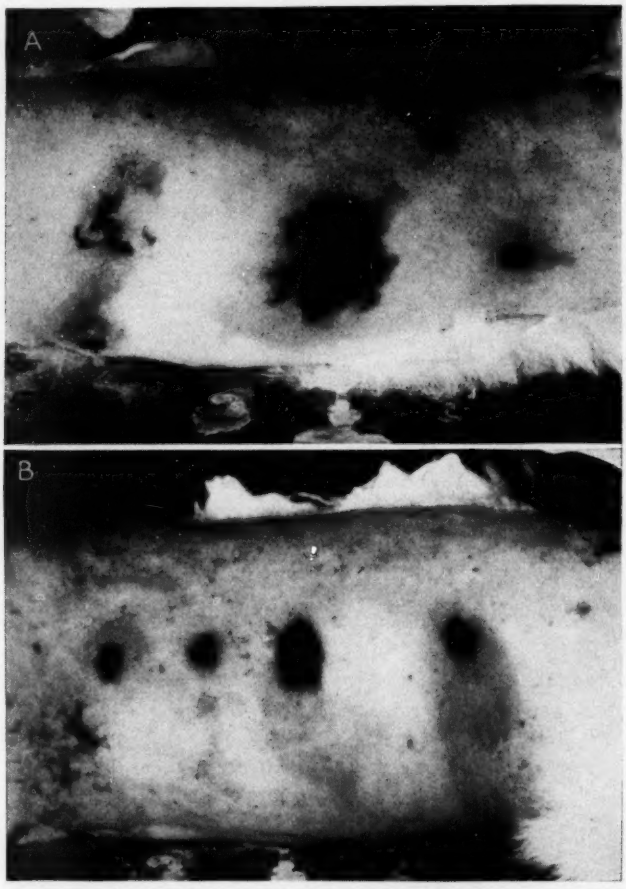

Fig. 3.—*A*, rabbit from "800" group (irradiated left flank). The spreads of the first and second injections are shown. The large lesion on the left was photographed five weeks after injection. The large lesion in the center was photographed 90 minutes after injection. The two smaller lesions represent the spread of the injections which did not contain hyaluronidase. *B*, same animal as in *A* (unirradiated right flank). From left to right, the first and third lesions were photographed five weeks after injection whereas the second and fourth lesions were photographed 90 minutes after injection. The larger lesions were produced by injections containing hyaluronidase.

7. The hyaluronidase was prepared from bull testes. The turbidity-reducing unit was defined as that amount of hyaluronidase which will just reduce the turbidity caused by 0.2 mg. of hyaluronic acid under appropriate conditions to that produced by 0.1 mg.

each flank (fig. 1). The injections were repeated similarly five weeks later, or six weeks after irradiation, in groups "control," "400" (fig. 2) and "800" (fig. 3). The second injections were given four weeks after irradiation to group "1600" (fig. 4) because the excessive roentgen therapy administered had been lethal within three weeks for 50 per cent of the group.

The spread of india ink was traced on cellophane® 5, 10, 15, 20, 30, 45, 60 and 90 minutes after injection and again 24 and 48 hours later. The spread at the end of 90 minutes was

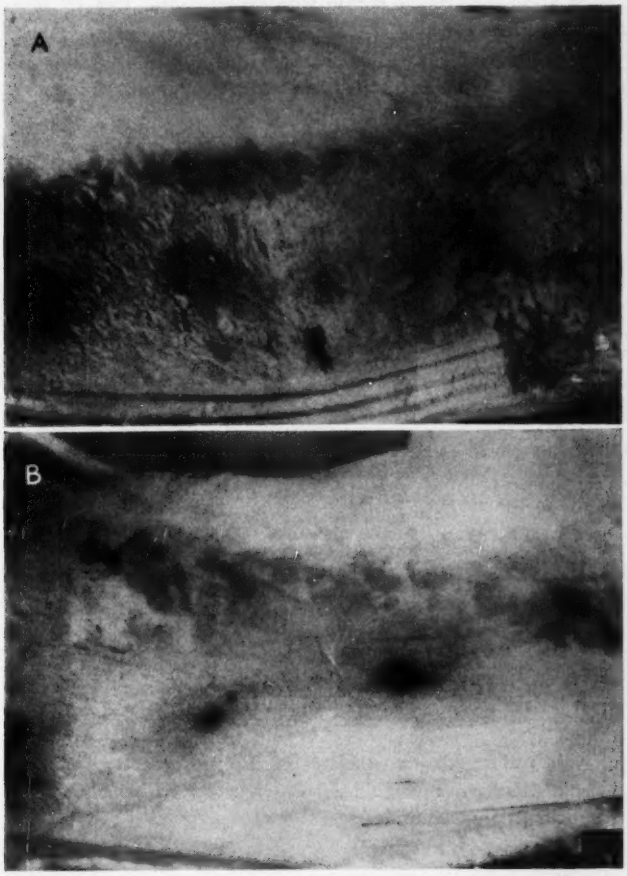

Fig. 4.—*A*, rabbit from group "1600" (irradiated left flank). This animal was photographed four weeks after it had been irradiated and 90 minutes after the second series of injections had been given. Evidence of radiodermatitis can be seen, and this has partially obscured the lesions produced. *B*, same animal as in *A* (unirradiated right flank). From left to right, the second and third lesions shown resulted from the first series of injections. Lesions one and four were produced by the second series of injections. The larger lesions were produced by injections containing hyaluronidase.

clearcut, and since further spread seemed to develop less rapidly thereafter this calculation was recorded. Each area of spread was determined by superimposition of the cellophane® tracings on millimeter-lined paper and counting of the enclosed square millimeters.

White blood cell counts and hematocrit determinations were carried out on groups "control," "400" and "1600" the week prior to irradiation and weekly thereafter for five weeks.

All results were analyzed statistically with the use of Fisher's "t" test.[8]

RESULTS

In table 1 are listed the results of all experiments. In groups including normal and irradiated areas the average spread with hyaluronidase was 3.9 times greater than that with sodium chloride.

The average totals for each irradiated group, determined one week after roentgen ray therapy was administered, showed no significant differences between

TABLE 1.—*The Effect of Roentgen Ray Therapy on the Average Millimeters of Spread of India Ink With and Without Hyaluronidase Injected Intracutaneously in Rabbits*

	Control Group (No Roentgen Therapy)				Experimental Groups *					
					"400"		"800"		"1600"	
	Square Millimeters of Spread	Standard Error			Square Millimeters of Spread	Standard Error	Square Millimeters of Spread	Standard Error	Square Millimeters of Spread	Standard Error
First Series of Injections †				First Series of Injections ‡						
Ink + hyaluronidase (left flank)	1,410	±	149	Ink + hyaluronidase (control flank)	1,085	± 101	742	± 175	1,231	± 332
Ink + sodium chloride (left flank)	396	±	58	Ink + sodium chloride (control flank)	387	± 32	206	± 38	581	± 43
Ink + hyaluronidase (right flank)	1,394	±	155	Ink + hyaluronidase (irradiated flank)	1,157	± 64	877	± 171	1,497	± 508
Ink + sodium chloride (right flank)	337	±	37	Ink + sodium chloride (irradiated flank)	476	± 53	233	± 42	438	± 75
Second Series of Injections §				Second Series of Injections ‖						
Ink + hyaluronidase (left flank)	1,789	±	94	Ink + hyaluronidase (control flank)	1,800	± 336	956	± 171	708	± 84
Ink + sodium chloride (left flank)	404	±	38	Ink + sodium chloride (control flank)	247	± 60	215	± 46	303	± 131
Ink + hyaluronidase (right flank)	1,671	±	194	Ink + hyaluronidase (irradiated flank)	1,808	± 366	1,151	± 164	905	± 413
Ink + sodium chloride (right flank)	328	±	29	Ink + sodium chloride (irradiated flank)	387	± 39	291	± 44	237	± 112

* One flank of each animal in groups "400," "800" and "1600" received 400, 800 and 1,600 r, respectively, in a single exposure.
† Results of initial series of injections in control group.
‡ Results of initial series of injections one week after irradiation.
§ Results of second series of injections. These were given five weeks after the first series.
‖ Results of second series of injections. These were given five weeks after the first series except in group "1600," in which the injections were given three weeks after the first series.

the spread with hyaluronidase on the treated flank as compared with that on the untreated flank. Similarly no significant differences were noted in the spread of injections utilizing sodium chloride.

The average measurements of the spread in both flanks of the control group did not vary appreciably.

The mean figures for the hyaluronidase injections in the "control," "400" and "800" groups obtained six weeks after roentgen ray exposure were greater than those obtained five weeks previously; however, this increase was not statistically significant. It could not be attributed to roentgen effect alone since the control

8. Fisher, R. A.: Statistical Methods for Research Workers, ed. 8, New York, G. E. Stechart & Company, 1941.

group exhibited a similar increase. The figures for the average spread for the sodium chloride injections after six weeks in groups "control," "400" and "800" were similar to those obtained at the end of one week.

All members of group "1600" manifested a diffuse erythematous, scaly dermatitis over the treated flank within one to two weeks after irradiation. The final injections were given to this group four weeks after irradiation (fig. 4). By this time only three of the six animals had survived the large dose of roentgen therapy. Although the mean spread of the second series of injections in the three remaining animals was less than obtained after the first series of injections, again the results were not significant statistically. No significant differences were noted in the individual animal in the comparative spreads over the irradiated and unirradiated flanks.

Peripheral leukocyte counts (table 2) and hematocrit determinations (table 3) were obtained on blood removed from the ear veins at weekly intervals in groups

TABLE 2.—*Average Leukocyte Counts (Ear Vein)*

	Control	"400"	"1600"
Initial count	7,415	8,050	9,285
1 week after roentgen irradiation	5,794	5,167	3,792
2 weeks after roentgen irradiation	5,667	6,475	4,000
3 weeks after roentgen irradiation	5,658	6,017	5,617
4 weeks after roentgen irradiation	5,417	6,983	6,483
5 weeks after roentgen irradiation	5,600	7,658	8,550

TABLE 3.—*Average Hematocrit Determinations on Peripheral Blood (Ear Vein)*

	Control	"400"	"1600"
Initial determination	45	42	41
1 week after roentgen irradiation	42	44	37
2 weeks after roentgen irradiation	42	44	28
3 weeks after roentgen irradiation	41	45	38
4 weeks after roentgen irradiation	41	44	40
5 weeks after roentgen irradiation	41	42	40

"control," "400" and "1600." The leukocyte count and hematocrit determinations did not vary significantly in the "control" and "400" groups. In group "1600" a significant temporary leukopenia and fall in hematocrit reading occurred within the first two weeks in all animals, including the three that survived.

COMMENTS

It should be noted that there were two sets of controls. The unirradiated side of animals in groups "400," "800" and "1600" served as a control for the individual animal. The control group received no roentgen therapy and therefore served as a control against possible systemic irradiation effects.

In the "control," "400" and "800" groups comparisons of the average spread of the first and second series of injections containing hyaluronidase showed the spread for the second series to be greater. In the "1600" group all the second series of injections had an average spread less than that of the first. None of these comparisons, however, when examined statistically, showed significant differences. It should be emphasized that in the "1600" group comparative differences were not significant even though the surviving animals had received sufficient roentgen therapy to kill

half of their group. The significant leukopenia and fall in hematocrit reading in this group would tend to substantiate the fact that three of the animals died of radiation sickness.

SUMMARY AND CONCLUSIONS

Roentgen therapy was administered in varying dosages to the left flank of 18 rabbits. A control group of six rabbits received no therapy.

Measurements were made of the spread of india ink plus sodium chloride and india ink plus hyaluronidase in both flanks of each animal one week and either four or six weeks after irradiation.

No significant differences were noted when comparisons were made within each group between the spread of ink with hyaluronidase in the treated and in the untreated flank, either one week after irradiation or later. Similarly, no appreciable differences were noted in the spread of india ink combined with sodium chloride.

These same observations were made even after the administration of sufficient roentgen therapy to kill half of one group. Death of the animals due to radiation effect was substantiated by significant rapid falls in the leukocyte count and hematocrit determinations.

It appears that within the first few weeks after the administration of roentgen therapy to rabbits the spreading effect of hyaluronidase in the skin is not significantly altered.

Miss Mary Virginia Stallworth gave technical assistance in the preparation of this paper.

ABSTRACT OF DISCUSSION

DR. A. FLETCHER HALL, Santa Monica, Calif.: Dr. Noojin's interesting experiment, although productive of negative results, is extremely provocative. It cannot but stimulate conjecture as to what mechanism is responsible for the beneficial effect of roentgen rays in the therapy of the pyodermas if, as his results would seem to indicate, the "spreading factor" hyaluronidase is not involved. But before the discarding of hyaluronidase as the instrumentality through which roentgen ray treatment accomplishes its beneficial effects, several possibilities which were not eliminated by this experiment suggest themselves.

1. Might there not be a demonstrable effect of roentgen irradiation on the spreading factor if such treatment were given in single or repeated fractional doses such as are ordinarily employed in the treatment of the pyodermas? It is conceivable, for instance, that such doses might stimulate the production of those antibodies which specifically inhibit the activity of hyaluronidase and which are known to be called forth by that enzyme. Larger doses such as were used in the experiment, on the other hand, might have no such effect.

2. Might there not be a demonstrable effect of roentgen rays on the spreading factor within 24 to 72 hours after the dose is administered? Early effects of roentgen rays have been demonstrated on the cellular activity of the male guinea pig nipple, and to me it is conceivable that the action of hyaluronidase might be altered within a day or so after roentgen ray administration, while that alteration might not be demonstrable a week later.

3. In certain particulars the conditions of this experiment do not parallel those which exist in the treatment of a pyoderma: in the latter instance, the hyaluronidase involved is of bacterial origin and in addition to calling forth specific inhibitory antibodies brings about an increase in the nonspecific hyaluronidase inhibitor which is present in the blood serum. All these factors are present and active before the roentgen ray treatment is administered instead of after, as in the present experiment. Is it not possible that there may be a roentgen ray effect on the hyaluronidase antigen-antibody system after it is already "in action," which does not occur when the roentgen ray dose is administered beforehand?

Because of my scanty knowledge of this subject and total lack of experience in animal experimentation, the questions which I have brought up were conceived in armchair contempla-

tion, and they perhaps can be disposed of in a few words. If, however, any of them have a true bearing on the subject, I hope they may be the basis for further experiments before Dr. Noojin abandons his interesting theorem.

DR. CHARLES C. DENNIE, Kansas City, Mo.: I might say that the effect of irradiation on embryonic tissue is immediate. This observation has been proved by the Canti film. Many of you saw it many years ago. The living chick embryo was subjected to the emanations from radium, and the dance of life stopped immediately. If the radium was used long enough the cells died. The activity of the macrophages also ceased. The wandering cells in the solution stopped temporarily but again slowly resumed their activity. Thus, on certain types of embryonic cells, the action of irradiation of any type causes the activity of those cells to cease immediately. The growth phenomenon is stopped immediately by irradiation, and, if the irradiation is strong enough, the cells die.

DR. RAY O. NOOJIN, Birmingham, Ala.: I should like to thank the discussants. We chose the doses that were used for a definite reason. Bloom (Histopathology of Irradiation from External and Internal Sources, [National Nuclear Energy Series, Manhattan Project, Technical Section, Division IV, Plutonium Project Record V22 I], New York, McGraw-Hill Book Company, Inc., 1948, p. 46) has pointed out the fact that it takes approximately 800 r to produce visible change in the skin of rabbits. Accordingly, 800 r were administered, and for comparative effects half and twice that dose were also given. Choice of the time interval before measurement of the effect of roentgen therapy was not entirely arbitrary. Wolbach (*Am. J. Roentgenol.* **13**:139-143, 1925) reported that the first changes in acute roentgen dermatitis of guinea pigs could be noted in the corium and subcutaneous tissues within two to three days after exposure to roentgen rays and that these changes reached a maximum in six to eight days. Therefore measurement one week after exposure was decided on. The six week interval was chosen in order for us to determine the comparative results of a more prolonged effect.

The subject of hyaluronidase is extremely interesting. The recent literature attests a wide interest in this material. Not only is this substance produced by mammals but also it is present in the venom of snakes and bees. Even some bacteria are capable of producing it.

Clinically, there is a possibility that a more thorough understanding of the activity of hyaluronidase may be of even greater importance in the future, since this enzyme is capable of reducing the viscosity of the tissue ground substance. Factors affecting the ground substance are of interest to dermatologists because of the profound changes therein occurring in lupus erythematosus and in certain other dermatoses.

SPLANCHNIC REMOVAL OF BACTERIA FROM THE CIRCULATING BLOOD OF IRRADIATED RABBITS

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AND
GRACE P. KERBY, M.D.
DURHAM, N. C.

THE EFFECT of roentgen irradiation on skin infections and on the spread of infection from local lesions has been studied extensively, and the studies have yielded variable results. This variableness is well emphasized in the excellent review article edited by Warren,[1] especially the portion by Dunlap,[2] on the effects of irradiation on normal tissues. It seems evident that there has been no method for obtaining completely satisfactory objective data, perhaps because of the many variables encountered. The variation in response from one animal to another, the changes of the response with the passage of time relative to the irradiation and the differences in the response with variation in roentgen dosage make the problem difficult.

Previous evidence [3] suggests that local infections may be altered in their invasiveness by local irradiation and that the ability of the animal to cope with any resultant

This work was supported by the Anna H. Hanes Research Fund and by a grant from the Duke University Research Council.

From the Division of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine.

Read at the Seventieth Annual Meeting of the American Dermatological Association, Inc., Jasper National Park, Alberta, Canada, June 20, 1950.

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2. Dunlap, C. E.: Effects of Radiation on the Blood and the Hemopoietic Tissues, Including the Spleen, the Thymus and the Lymph Nodes, in Warren.[1]

3. (*a*) Bloom, W.: Histopathology of Irradiation from External and Internal Sources, (National Nuclear Energy Series, Manhattan Project, Technical Section, Division IV. Plutonium Project Record, V22 I), New York, McGraw-Hill Book Company, Inc., 1948. (*b*) Benjamin, E., and Sluka, E.: Antikörperbildung nach experimenteller Schädigung des hämatopoetischen Systems durch Röntgenstrahlen, Wien. klin. Wchnschr. **21**:311, 1908. (*c*) Schwienhorst, M.: Untersuchungen über den Einfluss von Röntgenbestrahlungen auf die Kokkenphagocytose im Retikuloendothel, Beitr. z. path. Anat. u. z. allg. Path. **81**:375, 1928. (*d*) Schönig, A.: Über das Reticulo-Endothelialesystem unter Röntgenwirkung und seine Beziehungen zum Röntgenkater, Strahlentherapie **33**:55, 1929. (*e*) Teneff, S., and Stoppani, F.: L'influenza delle irradiazioni sulle linfoghiandole e sulla circolazione linfatica, Radiol. med. **22**:768, 1935. (*f*) Chrom, S. A.: Studies on the Effect of Roentgen Rays upon the Intestinal Epithelium and upon the Reticulo-Endothelial Cells of the Liver and Spleen, Acta. radiol. **16**:640, 1935. (*g*) Naiman, D. N.: Effect of X-Irradiation of Rats upon Their Resistance to Trypanosoma Lewisi, J. Parasitol. **30**:209, 1944. (*h*) Taliaferro, W. H.; Taliaferro, L. G., and Simmons, E. L.: Increased Parasitemia in Chicken Malaria (Plasmodium Gallinaceum and

bacteremia may be altered by either local or total body irradiation. It is not clear whether these possible effects are achieved through alteration of the invading bacteria or through alteration of the ability of the host to remove the bacteria once an invasion of the blood stream has occurred. The present study employs the venous catheterization method of studying the splanchnic removal of bacteria from the blood stream.[4] The studies were designed to note the effect on such splanchnic removal of the irradiation of the bacteria, both in the infected site before invasion of the blood stream and in vitro before injection into the animal, and of irradiation of the animal, both before and after the establishment of the infection. The basis for considering the possibility of detecting an alteration in the bacteria by a study of the development of a bacteremia secondary to dermal infection lay in previous investigations[5] which demonstrated striking differences in the efficiency with which various bacteria are removed in the splanchnic area and thus, perhaps, in the ease with which such a bacteremia can be established from a local site of infection.[5b]

METHODS

Healthy 2.0 to 3.5 Kg. rabbits were used. Anesthesia was maintained throughout each experiment by local procaine infiltration and by supplementary intravenously administered pentobarbital sodium as necessary.

The organisms used were a type 1 Pneumococcus obtained from Dr. Maclyn McCarty and a hemolytic, coagulase-positive Staphylococcus aureus of human origin. Pneumococcic bacteremias were obtained by the dermal infection method of Goodner.[6] Staph. aureus bacteremias were induced, as in previous studies,[4] by a continuous infusion of bacteria into the superior vena cava. Blood samples were obtained for culture by means of repeated cardiac punctures or inferior vena caval catheterization and hepatic venous catheterization. Blood samples were diluted with beef infusion broth when necessary to obtain countable plates.

Group 1, Staph. Aureus-Induced Bacteremias.—Controls were drawn from a previous study[5b] and constituted a group of 10 rabbits.

Five rabbits received 100 r (140 kv., 18 ma., 4 mm. Al filtration, half-value layer 0.5 mm. Cu and 20 cm. target-skin distance) through a 6 by 6 cm. port over the inner surface of the unshaved and unclipped hind aspect of the right thigh 48 hours prior to the induction of the Staph. aureus bacteremia.

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6. Goodner, K.: Further Experiments with the Intradermal Pneumococcus Infection in Rabbits, J. Exper. Med. **48**:413, 1928.

One rabbit received 800 r (factors as above) over the upper part of the abdomen, encompassing the liver and spleen areas, 56 hours prior to the induction of a Staph. aureus bacteremia.

Nine rabbits received 800 r (200 kv., 18 ma., 4 mm. Al filtration, 0.5 mm. Cu filtration, half-value layer 1.0 mm. Cu and 50 cm. target-skin distance) total body irradiation. The animals were restrained on a board and were rotated once in most instances from the prone to the supine position during the course of the irradiation. A Staph. aureus bacteremia was induced after irradiation in one rabbit at 49 hours, in one at 104 hours, in one at 9 days, in one at 12 days, in two at 22 days, in two at 27 days and in one at 30 days.

Group 2, Type 1 Pneumococcus Bacteremias Arising from an Induced Dermal Infection.—Controls were drawn from a previous study [5b] and constituted a group of nine rabbits studied 10 to 24 hours after the intradermal injection of bacteria.

Three rabbits received 200 r (140 kv., 18 ma., 4 mm. Al filtration, half-value layer 0.5 mm. Cu and 20 cm. target-skin distance) through a 6 by 6 cm. port centered over the shaved injection site in the right midabdominal region, at six, four and two hours, respectively, after the intradermal injection of bacteria. Studies were carried out 24 to 29 hours after the bacterial injection.

Seventeen rabbits received 500 r (85 kv., 5 ma., 0.85 mm. Al filtration, half-value layer 0.85 mm. Al and 4 inch [10 cm.] target-skin distance) through a 7 cm. round port centered over the shaved bacterial injection site in the right midabdominal region, two hours after the injection. Splanchnic removal studies were done on 11 of the 17 rabbits 23 to 29 hours after the injection, and for six of the 11 animals studies on paired nonirradiated control animals were run simultaneously. The remaining six of the 17 rabbits were paired also with nonirradiated control animals and were studied only from the standpoint of comparative intracardiac blood bacterial levels.

Three rabbits received 500 r (85 kv., 5 ma., 0.85 mm. Al filtration, half-value layer 0.85 mm. Al and 4 inch [10 cm.] target distance) through a 7 cm. round port centered over a point in the shaved right midabdominal region, at which site immediately thereafter bacteria were injected intradermally. The animals were paired with nonirradiated control rabbits and were studied 24 hours after the injection from the standpoint of comparative intracardiac blood bacterial levels.

Immediately before injection, half of the bacterial inoculum was layered thinly over the bottom of a small sterile Petri dish and exposed to 400 r (85 kv., 5 ma., 0.85 mm. Al filtration, half-value layer 0.85 mm. Al and 4 inch [10 cm.] target distance) through a 7 cm. round port which exceeded the diameter of the dish. One of each of three pairs of rabbits received this inoculum intradermally, the three control animals receiving the nonirradiated inoculum. Comparative intracardiac blood bacterial levels were determined in the paired animals 41 hours after the injection.

RESULTS

Group 1, Staph. Aureus-Induced Bacteremias.—The splanchnic removal of Staph. aureus in 10 control rabbits average 62 ± 20 per cent (S. D.).[5b]

The splanchnic removal of Staph. aureus in five rabbits irradiated with 100 r, 140 kv., over the thigh 48 hours previously averaged 67 ± 15 per cent (S. D.). This percentage does not differ significantly from that observed for the control group.

The splanchnic removal of Staph. aureus in one rabbit irradiated with 800 r, 140 kv., over the liver and spleen area 56 hours previously was 54 ± 13 per cent (S. D.), a figure again not significantly less than that for the control group.

The splanchnic removal of Staph. aureus in nine rabbits irradiated over the total body with 800 r, 200 kv., at varying periods prior to receiving Staph. aureus was as follows: one rabbit at 49 hours, 74 ± 12 per cent (S. D.); one at 104 hours, 62 ± 21 per cent (S. D.); one at 9 days, 87 ± 9 per cent (S. D.); one at 12 days, 72 ± 6 per cent (S. D.); two at 22 days, 66 ± 10 per cent (S. D.), and three at 27 to 30 days, 54 ± 17 per cent (S. D.). The differences from the control group were not significant.

No significant histological changes were noted in the livers of these animals when they were killed at the close of the experimental period of bacterial infusion. The spleens and bone marrows showed varying degrees of injury compatible with previously recorded irradiation effects.

Group 2, Type 1 Pneumococcus Bacteremias Arising from an Induced Dermal Infection.—The splanchnic removal in nine control rabbits average 8 ± 14 per cent (S. D.).[5b]

The splanchnic removal in three rabbits given 200 r, 140 kv., over the intradermal injection site at varying periods after the injection was —8 ± 16 per cent (S. D.) at six hours, 1 ± 11 per cent (S. D.) at four hours and 2 ± 16 per cent (S. D.) at two hours. These values did not differ significantly from those for the control group.

The splanchnic removal in 11 rabbits given 500 r, 85 kv., over the intradermal injection site two hours after the injection averaged 6 ± 10 per cent (S. D.) in five unpaired rabbits and 9 ± 16 per cent (S. D.) in six paired rabbits compared with 10 ± 20 per cent (S. D.) in the six control animals.

When six rabbits similarly irradiated were compared with paired controls as to intracardiac blood bacterial levels, no consistent difference between the irradiated and the nonirradiated animals was found.

In three rabbits given 500 r, 85 kv., over the injection site immediately before the intradermal bacterial injection, no consistent difference in the subsequent intracardiac blood bacterial levels could be noted on comparison with the three paired control animals.

In three rabbits given irradiated bacteria intradermally, no consistent difference in the subsequent intracardiac blood bacterial levels could be noted on comparison with the three paired control animals.

COMMENTS

By the venous catheterization method of study of the splanchnic removal of bacteria from the blood stream we were unable to demonstrate any effect of roentgen irradiation on the ability of the rabbit to clear the blood stream of bacteria by this splanchnic mechanism. With the dosages used, irradiation of a dermal infection site either before or after the infection was induced resulted in no apparent effect on the subsequent occurrence of a secondary pneumococcic bacteremia and in no apparent alteration of the animal's ability to cope with the established bacteremia. Similarly no effect on the subsequent occurrence of a secondary pneumococcic bacteremia was observed when the organisms were irradiated prior to their use in inducing a dermal infection.

When the factors and local irradiation site of Glenn [3k] were employed no effect on the subsequent ability of rabbits to clear the blood stream of continuously infused Staph. aureus was noted.

Total body irradiation in high doses had no observed effect on the splanchnic removal mechanism when Staph. aureus was continuously infused into the blood stream at intervals ranging from 49 hours to 30 days after irradiation.

The exact nature of the splanchnic mechanism for removal of bacteria from the blood stream is unknown. Most investigators have attributed the clearance of particulate matter to the activity of the reticuloendothelial system. Similarly the reticuloendothelial system is regarded as being particularly susceptible to damage

by roentgen irradiation. The liver appears to be somewhat less sensitive than the spleen. Ellinger [7] attributes the variability in results of studies of the liver after irradiation to a lack of uniformity of roentgen ray dosage and of time and method of observation of effect. In the present study, in which total body irradiation in high dosage was used and its effect on the splanchnic mechanism for the removal of bacteria was observed, no alteration of the liver could be detected either on histological examination or on observation of this particular hepatic function. If bacterial clearance is a function of the reticuloendothelial system, this result would indicate that the function of this system is not depressed by roentgen irradiation with the dosage used and over the period observed.

SUMMARY

By venous catheterization, with continuous bacterial infusion as described in a previous report [4] and the obtaining of bacteremias secondary to induced dermal infection, the effect of irradiation on the host and on the bacteria has been studied as it relates to the course of the bacteremia.

No alteration in the course of a secondary pneumococcic bacteremia was observed after irradiation of the dermal infection site either before or after the induction of the local infection.

Neither local nor total body irradiation in the doses used affected the splanchnic removal of Staph. aureus when this organism was infused into the blood stream at varying periods after the irradiation.

Dr. R. J. Reeves and the personnel of the Department of Radiology assisted us during the course of these studies, and Dr. B. Black-Schaffer of the Department of Pathology evaluated the histological evidences of irradiation effect.

ABSTRACT OF DISCUSSION

Dr. Wiley M. Sams, Miami, Fla.: Drs. Callaway and Kerby have reported the results of a carefully designed and executed experimental investigation which they have conducted in order to obtain objective data concerning the effects of radiation therapy on an infection with two common pathogenic bacteria. Their work reflects collaboration among the bacteriologist, pathologist, radiologist and clinician. They chose a method which would lend itself to an objective report, and they have subjected their results to statistical interpretation. Studies of variations between control groups and those animals subjected to various amounts of radiation therapy under the conditions imposed did not yield results with differences which were statistically significant. Bare figures can be notoriously dry, especially when the results are negative and particularly where glowing clinical reports lead us to believe that we should obtain some tangible and appreciable significant result.

It has long been accepted that radiation therapy has no immediate effect on bacteria in vitro unless the amount given is massive and intense. However, changes in inflammatory tissue following the administration of small amounts of radiation therapy are so frequently observed and the value of the treatment so widely accepted that a continued search to determine the mechanism and the method by which this result is achieved will always remain a subject of interest.

Though Drs. Callaway and Kerby were not able to show a significant decrease in numbers of bacteria it may, nevertheless, follow that some were destroyed, and the destruction of some invading organisms or an alteration in some of the inflammatory tissue which results from infection may be all that is necessary to alter the course of a given infection. The mechanism by which this favorable response is at times achieved, however, has not been satisfactorily explained. The splanchnic area of the rabbit involves tissues consisting chiefly of lymphoid,

7. Ellinger, F.: Response of the Liver to Irradiation, Radiology **44**:241, 1945.

endothelial and epithelial cells, which are relatively radiosensitive. Enthusiastic therapeutists, therefore, cannot criticize the experiment on the grounds that radiosensitive structures were not chosen.

Experienced clinicians choose for a therapeutic objective an established infection which has already provoked an inflammatory response. The Staphylococus infections were established after the roentgen ray therapy was given.

With the Pneumococcus bacteremia there were three rabbits that were irradiated, two, four and six hours after the infection was established, and in group C only two hours elapsed between establishment of the infection and irradiation. In group D the irradiation was given before the infection was established, and in group E the infecting organism was irradiated. These results, then, can hardly be used to decry our present clinical use of radiation therapy in well established infections where the products of inflammatory reaction have already manifested themselves by edema, infiltration, erythema and, perhaps, pain.

There exists an optimum time for the administration of radiation therapy for an inflammatory reaction. Irradiation too early or too late may result in failure to obtain maximum benefit. A study similar to the present one but in which the infections have been longer established might give results which would be of comparative interest.

Dr. Francis W. Lynch, St. Paul: Dr. Callaway was kind enough to provide me, before the meeting, with a copy of his paper, and reading it stimulated what had previously been a rather faint interest in the effect of roentgen rays on inflammations. None of us takes as much interest in this field as we might. We use roentgen ray therapy a great deal, and yet in recent years we have become so impressed with the results of chemotherapy and antibiotic therapy that we forget that we should go on with radiotherapeutic investigations. Most of us believe that roentgen rays have a favorable action against infection, but the evidence is conflicting and far from convincing. In ordinary dosage roentgen rays do not kill bacteria or viruses in vitro; in vivo action is unproved except in the case of a few organisms. Syverton has worked long in this field and believes that phagocytosis is probably not increased by roentgen rays in spite of some favorable reports.

Dr. Callaway shows that reticuloendothelial antibacterial action in rabbits is probably not enhanced by radiotherapy. If roentgen rays are effective in cutaneous infections how else may they act? Dr. Noojin (Hyaluronidase Action in Normal and in Roentgen-Irradiated Rabbit Skin, A. M. A. Arch. Dermat. & Syph., this issue) demonstrated that the spreading effect of hyaluronidase is not modified, but other enzyme actions may enter into the picture and deserve more study. Further study in that field may also contribute to the analysis of the effect of roentgen rays against noninfectious inflammations. Further study is certainly needed.

Dr. Callaway has applied an ingenious and apparently reasonably accurate technic to the study of cutaneous infection, and the fact that his observations fail to explain the mechanism of radiotherapy is by no means an unfavorable criticism of the value of the study. The practical elimination of various theoretic explanations makes it easier for subsequent experimenters to provide a satisfactory explanation for an influence of roentgen rays in cutaneous infections.

Dr. Fred D. Weidman, Philadelphia: It is axiomatic that in experimental work in general one should plan the experiments in such a way as to parallel as closely as possible the conditions which are obtaining clinically or otherwise. Dr. Callaway's work had to do with normal skin. However, in actual clinical work, in addition to the factor of the bacteria in the case, there is a reactive inflammation. One is dealing with a skin in which there is capillary dilatation and edema and more or less cellular infiltration. Theoretically, at least, the experimental results in an environment of that sort might be somewhat different from those in the present series. Thus, if Dr. Callaway is disposed to follow this matter further, I should suggest that prior to the application of the roentgen rays the skin should be inflamed by some nonbacterial means such as the application of turpentine or irritants of that order.

Dr. Stephen Rothman, Chicago: Like Dr. Lynch, I had the privilege of seeing the manuscript of Dr. Callaway in advance. I have been impressed by this painstaking work, and I am at a loss to explain the negative results obtained. I don't quite agree with Dr. Lynch that the therapeutic effect of roentgen rays on inflammatory processes is problematic. It certainly is not in erysipelas. In this condition fractional roentgen ray doses have proved to be curative and life saving in many instances. The effect is obviously on the tissue reaction and not on bacteria.

DR. HARRY L. ARNOLD JR., Honolulu, T. H.: It occurs to me that one of the things that Dr. Callaway has shown by his presentation is that he may have set himself a problem that was mathematically incapable of solution from the data. He has shown that there are two unknowns, and he has only a single method of solving the problem. It seems to me that the first unknown factor is the mode of elimination of the bacteria and the second factor, strongly suspected but perhaps unknown, is what effect roentgen rays have. I would suggest some possible approaches to that problem. One would be to compare the handling of dead bacteria with the handling of living bacteria, to at least eliminate the problem of the effect of growth of organisms during the period of the study.

Another would be the use of inorganic material, if some technic could be devised of measuring its removal from the blood stream, and I presume that would not be too difficult. A third would be the use of radioactive "tagged" material, following it to the point at which it is removed and perhaps by that means elucidating the curious paradox of the failure of roentgen rays to influence the removal of bacteria.

DR. EARL D. OSBORNE, Buffalo: I merely wish to point out another phase of this subject that I presume Dr. Callaway has given some consideration to. One of the theories of the presumed method of action of irradiation that has widest acceptance is that roentgen rays produce their effect through a shift in the acid-base equilibrium of the tissue. If that is true, examination of the blood, which is unaffected in its acid-base equilibrium, after irradiation is not going to show anything. It would be far more valuable to examine the tissues themselves, in which the infection exists.

I believe that a shift in acid-base equilibrium, from the acid to alkaline, explains many of the events following the use of irradiation in cases of infection.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I am wondering how much the adrenal glands may have been affected by the irradiation to the splanchnic region as used in these experiments. Recent evidence indicates that adrenal secretions profoundly influence the course of infections and tend to suppress many of the systemic reactions that are usually associated with them.

DR. J. LAMAR CALLAWAY, Durham, N. C.: A point that Dr. Brunsting brought up was one that concerned us a great deal. We recognize that the adrenal glands in the rabbit are spread over the entire abdomen. In view of the dissemination of the tissue, we knew of no way to keep from irradiating the adrenal glands indirectly. Our previous experience involved rabbits, on which we had extensive experimental data. For this reason, we could not use mice or rats, which under the circumstances might have served as better experimental animals, had we been able to catheterize them.

I should like to take this opportunity to thank Dr. Sams and the others who discussed this paper for their helpful criticisms and comments. We shall attempt to follow out their suggestions.

ECZEMA

A Psychosomatic Study

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THIS STUDY deals with that large group of skin disorders known variously as eczema, atopic dermatitis, neurodermatitis and lichen simplex. It is estimated that one third of all patients with skin disorders have diseases of this group, which are noted for chronicity, refractoriness to treatment and multiplicity of etiological theories. The purpose of this study is to answer the following questions: What type of person has eczema? What emotional factors, if any, precipitate the disorder or cause relapses? Can psychotherapy help these patients?

No pretense is made that physical factors are unimportant. Few patients were seen whose skins had not at some time reacted to a harsh soap or a specific allergen. Many were seen who had made good recoveries under routine treatment. Many more were seen who had relapsed again and again and trekked from hospital to hospital without lasting relief.

MATERIAL

The 90 patients whose cases form the basis of this study were observed in Army and civilian practice. Seventy-one of them had eczema or atopic dermatitis, and 19, neurodermatitis.

Thirty-seven Army patients were seen by one of us (E. W.) in several British military hospitals; they were interviewed for at least two hours. These patients were a random sample, selected only in the sense that they were all of an age and physique for active military service and that they had been sufficiently disabled by their skin disorder to warrant referral to a dermatologist by their unit medical officers. Fifty-three civilians were psychiatrically examined for an unrestricted period by us and our colleagues in the Skin Department of St. Bartholomew's Hospital in the eighteen months following April 1948. During this period 585 patients of the "eczema family" passed through the department. Thus the persons seen were twice selected—first, by the family physician, who had probably tried his own treatment before referring them to a hospital, and, secondly by the dermatologist, who tended to refer patients who displayed some abnormality of behavior or those who had proved resistant to "routine treatment."

The Army group were more homogenous with regard to age, sex and duration of illness than the civilian group (see table 1). It is assumed that persons with conditions of long duration or "childhood" eczemas such as appear in the civilian group would have been excluded from the Army by enlistment medical screening. To render observations on the group comparable with those for the "controls" information on 9 individuals—officers and women's service personnel—was dropped in table 1.

From the Department of Dermatology, St. Bartholomew's Hospital, London.

Dr. Wittkower is psychiatrist to the Dermatological Department, St. Bartholomew's Hospital, London, Dr. Edgell Clinical Assistant, Dermatological Department, St. Bartholomew's Hospital, London, and C. Rutherford Caverhill Fellow in Medicine of McGill University, Montreal.

The control series consisted of 50 "war wounded" examined at random for another purpose. These were considered to be a fair cross section of the British Army. The two hour interview was directed particularly to their psychiatric history, so that figures relating to physical disease must be taken with reserve.

OBSERVATIONS

Statistical Summary of Observations.—A glance at table 2 shows that eczema patients as a whole differ from the control group in their constitution, childhood environment, health (both physical and mental) and general personality development. These differences were most pronounced in the 18 patients who had had eczema from childhood, and they could also be demonstrated by culling a group of 50 in whom there was a clear association between significant emotional stimuli and onset or relapses of their eczema (50 "superselected" patients).

Precipitating Situations.—A correlation between emotional disturbances and eczematous manifestations could be established in 77 of the 90 patients studied

TABLE 1.—*Age and Sex Distribution and Duration of Illness*

	Controls (Army Wounded)	Army Averages	Unselected Army Eczema Patients: Total	Unselected Army Eczema Patients: Less Women's Service Personnel and Officers	"Super-Selected" Eczema Patients	Total No. of Eczema Patients
No.	50	..	37	28	50	90
Sex	All M	..	35 M, 2 F	All M	37 M, 13 F	63 M, 27 F
Age:						
Under 20	10%	7%	6%	6%	8%	10%
21-30	68%	46%	43%	47%	48%	35%
30 +	22%	42%	51%	47%	44%	55%
Duration of illness						
Since childhood	..	..	3%	0%	24%	20%
10 years +	..	..	8%	8%	12%	12%
2-10 years	..	..	46%	46%	40%	41%
1-2 years	..	..	37%	39%	18%	19%
"Months"	..	..	6%	7%	6%	8%

(30 of the 37 Army patients and 47 of the 53 civilian patients). Events of a disturbing nature preceded the onset of the malady in 46 cases. In 31 the onset was too distant, too ill defined or too much complicated by other factors to allow an appraisal of the relevance of emotional factors. Altogether, 174 episodes could be isolated in which onset, relapses or aggravations of eczema were clearly related to emotionally disturbing situations. These situations could be grouped under one or several of the following headings:

A. Threats to Life and Existence: About one quarter of the episodes concerned physical safety. In the Army group, as might be expected from the nature of service life, the bulk of threats were in terms of bombs and bullets; in the civilian group were many other factors, such as loss of job and impoverishment.

CASE 1.—J. G., a clerk aged 40, was the youngest of three children and always came off on the short end. His elder brother and sister got the better education and the better jobs. His ambition was to "create something" with his hands; yet he had to shelve his aspirations in order to support his widowed mother. As a baker's roundsman he constantly worried about business being bad and the possibility of his dismissal. It was in this setting that his dermatitis started when he was 28 years old.

It persisted on and off for several years. Prior to his enlistment in the Royal Air Force he had a relapse; afterward he was "miraculously" free from skin eruptions. Service conditions suited him down to the ground because for the first time in his life he could do what he really

TABLE 2.—*Comparative Summary of Relevant Features in the Histories of Fifty Controls and Ninety Eczema Patients, the Latter Subgrouped Also As "Army Unselected," "Childhood Eczemas" and "Superselected"* *

	Heredity	Wounded Controls (50 Patients)	Army Unselected Eczema Cases (28 Patients)	Childhood Eczema Cases† (18 Patients)	"Super-Selected" Eczema Cases (50 Patients)	Total Eczema Cases (90 Patients)
1	Eczema or other skin manifestation in family	0%	21%‡	28%‡	30%‡	21%‡
2	Asthma, bronchitis, tuberculosis, pneumonia	6%	21%	17%‡	26%‡	14%
3	Other possibly psychosomatic disorders	6%	14%	28%‡	24%‡	19%‡
4	Total "psychosomatically tainted" heredity	12%	21%	44%‡	50%‡	38%‡
5	Psychoneurotic, mental defective or psychotic	30%	43%	39%	38%	37%
	Childhood					
	Position in Family					
6	Eldest	18% (of 44)	20% (of 20)	28%‡	16%	18%
7	Youngest	25% (of 44)	25% (of 20)	22%	34%	30%
8	Only child	23% (of 44)	20% (of 20)	33%‡	16%	15%
9	Other	34% (of 44)	35% (of 20)	17%‡	34%	37%
	Security					
10	Deprivation	16%	14%	44%‡	26%	35%‡
11	Overprotection	18%	32%	39%‡	40%‡	32%‡
12	Total percentage "out of balance"	34%	46%	83%‡	66%‡	67%‡
	Orientation					
13	Mother-oriented	32%	43%	61%‡	54%	53%‡
14	Father-oriented	6%	7%	11%	18%	14%
15	"Evenly balanced" in orientation	62%	50%	28%‡	28%‡	33%‡
	Health					
16	Physically "delicate"	4%	43%‡	56%‡	38%‡	30%‡
17	Neurotic traits	34%	50%	44%‡	46%	42%‡
	Adulthood					
	Health					
18	Other skin disorders or responses	2%	67%‡	....	44%‡	38% (of 86)‡
19	Asthma, bronchitis, tuberculosis, pneumonia	0%	21%‡	....	38%‡	27% (of 86)‡
20	Other psychosomatic disorders	16%	29%	....	29%	39% (of 86)‡
21	Psychoneurotic manifestations	10%	39%‡	....	82%‡	90% (of 86)‡
	Sexual Adaptation					
22	Sexual performance "unsatisfactory"	20%	47%‡	....	64%‡	55% (of 86)‡
	Marital status	Army Average				
23	Married, widower or separated §	55%	42%	64%	....	62%‡	68% (of 86)‡
24	Single §	45%	58%	36%	....	38%	37% (of 86)‡
25	Average age (years) at marriage	24 (of 20)	24.7 (of 17)	....	26 (of 31)	25.7 (of 51)
26	Percentage with wife in ill health or dead	9% (of 21)	37% (of 16)	....	32%‡ (of 31)	37% (of 54)‡
	Social					
27	Inhibited in social contacts	30%	50%	....	54%‡	46% (of 86)‡

* The figures in table 2 have been statistically validated by the determinations of chi-square and the standard error of difference between per cents.

† It should be noted that the group of "childhood eczemas" is too small for accurate comparisons.

‡ A significant difference between patient and control groups is indicated by the double dagger.

§ In items 23 and 24 the groups have been compared with "Army averages" rather than the controls.

liked to do, i. e., work as a fitter, and because he was without responsibilities or worries for the future. After he had had two years of service his right hand was accidentally amputated by an airplane propeller. Subsequently he was discharged on an 80 per cent pension.

Since it was impossible for him to carry on in any occupation which required manual skill he then took a dead end job as booking clerk in a tramp's refuge. At this institution he felt unhappy and frustrated. Moreover, he had to work in a tiny office with windows on three sides. After

the institution had been hit by a flying bomb, the skin malady flared up on his left arm. This incident raised acute anxiety in the patient regarding the possibility of an injury to his good arm. He had another relapse after some disaffected ex-inmates had smashed a window of his office.

B. Threats of Loss of Outside Sources of Support: About two fifths of the episodes seemed to relate to actual or threatened loss of a much needed key figure in the patient's environment, either by death or departure or by withdrawal of sympathy with the patient's mode of behavior.

CASE 2.—J. C. B., aged 36, had an unhappy childhood in a poverty-stricken home with a heavy-drinking, brutal father. He grew up quiet, shy and timid. At 26 he married and found his first real security and comfort. His wife and his home were everything to him; he hated joining the Army and dreaded being sent overseas. He was posted to India; a month after his arrival the eczema started on one foot. For a year he was in and out of Sick Quarters and on light duty. He feared that he might be sent to Burma and manifested gross anxiety symptoms. The eczema gradually became worse. In the base hospital, when repatriation was suggested, the condition of his skin improved; when his departure was delayed he had a relapse. On return to England he improved but relapsed when put back on full duty.

C. Threats to Inner Established Patterns: Precipitating episodes which proved to be threats to an established emotional pattern within the individual included blows to self esteem, situations arousing sexual conflict and those stirring up latent aggressiveness.

Blows to self esteem were found to be operative in about a third of the episodes. The majority concerned social and vocational performance, failure to maintain a level of professional or social achievement or demotion.

CASE 3.—F. A., retired at the age of 69, had always thrived on his popularity. He reveled in his past successes as a businessman, sportsman and ballroom master of ceremonies. After a very hard struggle he had managed to build up a flourishing ladies' outfitting business; at the height of its success he had 13 employees. Gradually, in the years after the 1914 war, the business went down and he had to sell out. After he had paid all his debts he was left with practically nothing. Within a few weeks of this disaster he started to have eczema. It cleared up for a few years while he was successfully running an agency for a foreign firm. It came back when this firm went bankrupt. Since then he has gone downhill financially and the condition of his skin has deteriorated. He is now dependent on his wife's earnings.

Sexual conflict seemed to occur in about a fifth of the episodes. Emotional tension aroused by such events as engagement, marriage, the wife's pregnancy or an extramarital affair was often seen to originate from remnants of an infantile child-parent relationship carried over into adult life.

CASE 4.—G. L., an unmarried woman aged 26, had loved only one man—her father. He had been a hard-working, debonair barber and had worn a well groomed mustache. He had died when the patient was 10. She grew up to be a prim, proper, sexually inhibited girl. She had been frightened as a child by the efforts of her father's mustachioed customers to steal an occasional kiss. At the age of 18 she had a frightening encounter with an exhibitionist in a blackberry patch. On the following day one of her companions had a swollen mouth and was said to have been "poisoned by the shock."

As an Auxiliary Territorial Service conscript she enjoyed life very much until, at a Christmas party, she was kissed by a soldier who had always been repugnant to her. She had jestingly said that his mustache was "full of germs." On the following morning her mouth was swollen, and an eczema of the upper lip followed.

Latent aggressiveness was relevant to about one quarter of the episodes. This was a particularly potent force when directed against otherwise loved figures in the environment—"mingled feelings," the hostile aspects of which the patient dared not express.

CASE 5.—N. T., a professional musician aged 31, had a discoid eczema of the hands that prevented him from playing his cello. It came on when he was demoted in the orchestra to make way for a rival cellist who had also been a rival in love.

This situation was not unfamiliar to the patient. As a second son he had, in childhood, resented the priority of his elder brother. His father ignored him. His mother doted on him and encouraged him to take up her profession, music. Jealous of the attention his mother lavished on boy pupils, he staged "suicides" and had several serious accidents, often involving his hands—the hands that were being cherished for a musical career. He would strangle his pet dog under the guise of scientific experimentation. He rejoiced in the possession of a small bore rifle with which he killed a sheep.

Later on, as a pilot in the Air Force, he carried a service revolver and enjoyed the feeling of power conveyed by a bank of machine guns under his thumb. He was a small man and rarely allowed his pent-up aggressiveness to be expressed in fighting. He had one serious love affair and was jilted. In revenge on womankind he got a nursing sister with child and then married her in remorse.

He had nothing in common with his wife, and the marriage was a source of continual frustration. His temperamental difficulties hazarded his musical career. Rejection by the orchestra director realighted the childhood conflict over the rejecting father, and ungovernable but inexpressible aggression resulted in the onset of his eczema.

During treatment several relapses were directly associated with quarrels with his wife; he confessed to the urge to strike her. Two recurrences followed stag parties in which his latent homosexual conflicts were stirred up. The treatment made it clear that his choice of musical instrument was neurotically determined—a sublimation of autoerotic urges. He lost the desire to play, quit his wife and his profession and rejoined the Air Force. His eczema flared up as the end of the treatment was approached and then subsided.

PERSONALITY DEVELOPMENT

As can be seen, the factor common to all these precipitating episodes is a threat to security, external, or internal, or both. For one to understand the full significance of this observation, the total personality of the patients investigated must be taken into account.

Constitution.—In accordance with the generally accepted observation of a hereditary predisposition to eczema, our patients show an incidence of skin disorders in the family of 21 per cent, with one of 28 per cent in those who developed eczema in childhood. A high number of patients in this group were of the "vasomotor skin type"; i. e., they responded disproportionately, with their skins, to situations evoking feelings of fear or embarrassment. The eczema patients also seem to show a family predisposition to respiratory disorders (14 per cent in comparison with 6 per cent) and to such "psychosomatic" disorders as peptic ulcer, hypertension, arthritis and diabetes (19 per cent in comparison with 6 per cent in the control series). (See table 2.)

Childhood Environment.—It has been observed by Rogerson, Hardcastle and Duguid [1] that the "difficult" positions in the family prevail in asthmatic children. In our patients with childhood eczema, likewise, it has been found that a larger than average proportion of persons fall into the stressful "difficult" positions—the

1. Rogerson, C. H.; Hardcastle, D. H., and Duguid, K.: Guy's Hosp. Rep. **85**:289, 1935.

oldest child, who bears the strain of responsibility or of competition with younger siblings; the only child, who lacks the stimulus of competition and has the undivided attention of his parents, and the youngest child, either running to keep up or too discouraged to try to keep up. "Difficult" positions were, however, not predominant in those patients who started to have eczema in adult life (see table 2).

The stresses of childhood can best be understood in terms of "psychological needs." A child needs the security and backing, love and understanding of two present parents, an optimum period of gratification of infantile desires and opportunities to express hostilities. Both too little and too much satisfaction of these childhood needs may lead to stress and, in consequence, to a sense of insecurity and feelings of anxiety.

Sixty-one of our eczema patients had had, or felt they had had, either too little or too much gratification of their childhood needs. Thirty-five of the 61 felt that they had been "unwanted" as children. Among them were those who had grown up in homes broken up by death, desertion, separation or departure, those whose childhood had been marred by quarrels and fights between their parents or the violence of a heavy-drinking father and those who were obviously unwelcome youngest children. Of the 26 "spoiled" patients 12 had been "Benjamins" and the remainder only children, only boys among girls or favorites for some other reason.

Childhood Behavior.—The bulk of these patients described themselves as having been shy, anxious, introverted children. They were usually unaggressive and shrank from new contacts and new experiences. Though studious and sometimes of above average promise, they often "flunked" examinations and rather rarely achieved the goal they had set out for. They clung to the well remembered and relatively safe—the parents, the home, the very behavior of infancy.

A minority, about one quarter of the total, concealed their sense of insecurity by overcompensatory aggressive, stubborn or obstreperous behavior, displayed temper tantrums or even committed acts of minor delinquency.

Adult Behavior.—As the insecure child faces the problem of how to grow up without losing his equilibrium, two courses are open to him: Either (*a*) he can retain his childlike dependent clinging qualities, leaning heavily on his parents or their substitutes or (*b*) he can further develop the process of overcompensation and cover his basic insecurity with a facade of defense reactions.

The latter technic of "disguise" is the more commonly adopted by those who were "unwanted" children. It is as though they had said to themselves, "This policy of polite passive subservience is not getting us anywhere; let's try the opposite tack." The onetime "spoiled" children were more likely to retain "undisguised" childlike traits, as though to say, "We were always able to lean in the past; why not now?"

In 74 adult patients with (clearly psychosomatic) eczema, "undisguised" behavior types numbered 28. The "disguised" included 21 "resentful" patients, 15 "self drivers" and 6 "limelight seekers." Four could not be classified.

The diagnostic interview provided a good test situation in which to watch the patient's behavior.

The "undisguised" eczema personality may appear quite obviously childlike and immature. Commonly the patient appears to be younger than his years.

favoring juvenile dress and simplicity of manner and makeup. The married family man may wear sports clothes in midwinter, the city typist of 30 a baby ribbon in her bobbed hair. They are characteristically well dressed, good-looking, likeable people. They like to be liked. The good will and approval of others is everything to them, and they cultivate good will assiduously.

They are reluctant to expose their own feelings lest they prove offensive to the interviewer. They resemble the well behaved child who speaks only when spoken to. Their anxiety about the interview may have been such that wife or mother has accompanied the patient and is appealed to helplessly for dates and details. This lack of spontaneity delays the interview process, but when rapport with the doctor has been achieved these patients readily transfer their dependent leanings on to him.

The "resentful" type may be palpably hostile, suspicious and uncooperative. Patients of this type have quite often been sent along by an exasperated dermatologist without any explanation. Referral to a psychiatrist is often interpreted by them as a deliberate slight, and this is added to the lengthening list of accusations against physicians in general. Just as they resented their childhood dependence on their parents, so now they resent the need to bring their problems to a physician. Or such patients may superficially appear calm, poised and friendly. The underlying tension and repressed anger may be betrayed only in the rigidity of their muscular armour. The calm face is really a frozen mask; the poise is not that of relaxation and comfort but of tenseness to resist attack; the hands are not folded but clenched. The speech may be, not hesitant with respect, but, rather, inhibited by fear of letting go. There may be an actual stutter, or a voluble overflow, replete with aggressive allusions.

"Self drivers" and "limelight seekers" appear in the interview as successful men of the world—apparently poised and at ease, self assured, perhaps slightly patronizing. The disguises cover an essential unsureness of which they may be vaguely aware. Often they have extended themselves beyond the point of comfort, and, like the resentful ones, they may betray a dim perception of their vulnerability by a blush or a trace of perspiration, a tremor or an involuntary itch and scratch when the investigator treads on dangerous ground.

These visible clues to the location of focal conflicts can often be observed during the interview. Typical of many others is the following case:

A girl of 4 was being interviewed with her mother. Her eczema had started at 3 weeks, when she was weaned through blitz necessity. It recurred at 2½, when sibling rivalry became intense. The eczema had decreed that the mother would go to bed with the child (to the exclusion of her husband for 1½ years!) and for an hour each night rub the child with soothing ointments. When the doctor queried the suitability of these sleeping arrangements, the child started to whine and scratch and the mother proceeded to anoint the child on the spot, with immediate relief.

SOCIAL AND OCCUPATIONAL ADJUSTMENT

The well documented groups of 28 Army eczema patients and the controls provide an opportunity for some statistical comparisons (table 3). Though rather fewer of the eczema patients had volunteered for the Army, rather more of them seemed to "settle down." They had a better "crime" record as a group. In spite of these favorable factors, the eczema patients obtained only half the average amount

of promotion or offers of promotion—22 per cent as against 40 per cent. The eczema patients declared a high incidence of "shyness" in social contacts—50 per cent as against 30 per cent.

Among the "undisguised" eczema personalities are the "stay-at-homes" and the "wallflowers"—all is well with them as long as they are able to stick to a well accustomed pattern of life. They are inelastic and inadaptable. Anything out of the ordinary is to them an intolerable strain. They are late to embark on a new way of life, such as marriage or a new job, and show a preference for "dead end" secure pensionable positions. Thus a woman, aged 36, had remained in a poorly paid job with one firm for 16 years because a change appeared to her hazardous, had postponed matrimony until she was 34 because she could not tear herself away from her overprotective possessive mother, had brought her husband home to live with her mother, and manifested eczema when her conflicting loyalties, metaphorically and literally, gave rise to friction.

TABLE 3.—*Adjustment to Army Life of Eczema Patients and Controls*

	Army Eczema Patients (28)	Army Controls (50)
Conscripts	22 (78%)	34 (68%)
Volunteers	6 (22%)	16 (32%)
Average duration of service	4.3 years	4.0 years
"Liked the Army"	9 (32%)	11 (22%)
Acceptant—compliant	6 (22%)	13 (26%)
Disliked the Army	13 (46%)	26 (52%)
Charges		
One	6 (22%)	4 (8%)
Several	1	7 (14%) } (24%)
Many or major	1	5 (10%) }
Promotion		
Granted	5 } 6 (22%)	12 } 20 (40%)
Offered but refused	1 }	8 }
Demoted	1	3

Under the normal pressure of home or office these persons are likely to "get all het up," with the result that their efficiency is impaired. "I just can't get through my housework. I'm so slow," moans the daughter-in-law of a neurotic tyrant who rules the common kitchen. "When the boss gives dictation I get all trembly," says the stenographer.

A lower level of achievement is commonly found than might be expected from the background and apparent intelligence of the patient. "All my brothers and sisters are well educated and have got on in the world," said a woman of 28. She was the ninth child and had worked for 10 years as a packer in a canning firm.

These patients are usually inoffensive individuals. Hostile feelings toward a key figure in the environment are particularly intolerable and a source of guilt and anxiety. Typically, one of our female patients manifested eczema at the age of 14, when, after the remarriage of her widowed father, her stepmother gave birth to a baby. To all appearances she was utterly devoted to this child, but her anxious overconcern about his well-being flimsily concealed hostility for a rival.

Such persons readily assume that they are "not wanted" or "failures." To cover up their inferiority feelings they often bite off more than they can comfortably

chew, and then, having met a setback, they get flustered or discouraged and stop trying. They may take the line of least resistance and quit when the going gets tough (see case 5).

The "disguised" eczema personalities are those who, having perhaps dimly perceived the incompatibility of their basic natures with adult status, overcompensate by the development of precisely opposite surface characteristics.

The "limelight seekers" are the life of the party, full of bonhomie and apparent ease of manner. Frequently in their choice of activity they twist their inner lions' tails! Thus a youth with conflicts over sexuality entertained at parties by female impersonations, and a professional footballer felt his underlying uncertainty assuaged by the approving roars of thousands.

"Self drivers" would seem to have chosen the most useful and socially acceptable mode of behavior though not necessarily a better solution for the problem of their own equilibrium. They frequently set themselves goals beyond their comfortable grasp, with high standards of ethics and performance which keep them in a state of striving anxiety. Their motive may be to outdo a despised parent or to emulate a loved one. They often achieve pinnacles of success but may find them slippery slopes. They may push themselves into a state of nervous exhaustion or into illness, and they have no reserve to meet the routine crises of business.

Typical is the case of a man, aged 59, who had worked himself up from the humble position of a junior clerk to that of a managing director of a large firm. Material prosperity had brought him no happiness because he continually felt insecure in himself. He always anticipated misfortune. His first marriage ended tragically; without warning his wife left him for another man. While he was smarting under the injury which she had inflicted to his self esteem, his eczema started. Subsequent relapses were preceded by the loss of another loved person (the death of his son) and business crises (the need to make crucial negotiations with risk of loss). His new wife, though 15 years younger than he, mothers him a good deal. His unjustified fear of losing her is increased by his deficient potency.

Patients of the "resentful" type have failed to canalize their energies usefully. Their resentment is rarely openly expressed for fear of incurring hostility from without and of adding to their feelings of depression and anxiety. These feelings, if projected into the outer world, may give rise to ideas of persecution. If they can "blow off steam" their tension is relieved, but more often than not patients of this type "flush with anger," walk away and tear the strips off themselves which they would like to tear off others.

SEXUAL AND MARITAL ADJUSTMENT

Exploration of the early adult sexual life of the patients in this series shows, perhaps more often than usual, anticipatory anxiety, obsessional doubts, fear of situations out of control and oversensitiveness to rebuff. All these factors make for disinclination to participate in heterosexual social activities; a rare individual overcompensates by Don Juan or "tart"-like compulsive promiscuity. Altogether 55 per cent of these patients had made an inadequate sexual adjustment, with such characteristics as persistent autoerotic practices, inhibited sexual interest, impotence, premature ejaculation and frigidity.

Marriage in these cases is rarely founded on a sound and stable basis. Not infrequently patients in this series, unrecognized by themselves, had chosen husband

or wife in the hope of perpetuating or recapturing a state of childhood dependence. "We are sitting on each other's laps," said a boy of 27 who had recently married. A businessman, aged 46, could resist his urge to scratch himself only if his wife, a very motherly type of woman, sat by his bedside and held his hand. She described him as her third child.

Such alliances were likely to arouse conflictful remnants of son-mother or daughter-father relationships. Many a married patient was as fixed on his partner as he once was on his parent. The husband would grudge his wife any activities which did not include him. The advent of children might arouse a fierce "sibling rivalry." A jealous father would scratch furiously when the baby cried in the night, so that the wife had to turn to him with comfort and soothing applications. Similarly some women could not tolerate their husband's preoccupation with business, sports or hobbies. "When he goes off on Saturday afternoons with his golf clubs I just tear myself to pieces." The need for security decreed that the partner should be an ideal figure. This view might blind a husband or wife to the other's failings. He or she might cherish a rosy ideal for years and suffer only when face to face with bitter reality.

ADJUSTMENT TO ILLNESS

Most patients suffering from eczema are concerned about their appearance. The conviction that they must be repulsive to others reenforces their premorbid seclusiveness. "I don't care to go out," "I see people turn their faces away," "I feel self conscious" and "It's not nice to scratch when people see you," they often say. Many feel "dirty" or afraid of having a contagious or hereditary disease. Embarrassing comments in a barber's shop, the shrinking of a partner at a dance or the advice of a well meaning friend may accelerate their social withdrawal. Actual ostracism is not uncommon, as in the case of the girl who was debarred from teaching and from organ playing on account of the potential "infectiousness" of her disease.

The eczema irritates or itches sometimes to the point of interference with the patient's occupation and rest. Pruritus may precede the development of eczematous eruptions so that in some cases one may well wonder whether the eczema caused the itch or vice versa. However troublesome, skin irritation rarely drives patients to desperation—only two said they had ever felt like committing suicide.

Anxiety and guilt may be roused by the secondary effects of the disability on others. The housewife who cannot put her hands in water may worry as she sees her husband bathe the baby; the husband may guiltily watch his wife striving to remove ointment stains from his pillowcase or scabs from the carpet.

PSYCHOLOGICAL TREATMENT

Dermatologists are agreed that these patients are baffling and often refractory to treatment. There is no "standard treatment." The ointment which suits one patient will not suit another and may even aggravate the condition of the same patient at a later relapse. Allergic and dietary factors fluctuate bewilderingly. Any new ointment or any new physician is likely to be successful, but only for a short time. As with peptic ulcer and asthma, eczema is a disorder in which the multiplicity of "successful" treatments is the only "standard" thing. When this

situation exists it is probable that such factors as faith in a "new cure" or in the physician who prescribed it are partly responsible for the success.

The common observation that endogenous eczema dramatically subsides with hospital treatment, only to recur on return to the outside world, is readily understood in view of the basic characteristics of the sufferers. In hospital they are relieved, at least to a certain extent, from their cumbersome responsibilities. They are looked after by parent substitutes in the shapes of physicians and nurses. Compresses and ointments are applied to them in a situation analogous to their dimly remembered infancy when they were caressed, nurtured, bathed, oiled and powdered.

On the assumption that institutional or accidental psychotherapy is effective in this manner an attempt at deliberate and systematic psychotherapy seemed to be justified. Of the 53 civilians, 34 patients were selected for this pilot research; 19 were rejected for the following reasons: The psychosomatic connection either was not apparent or was too deeply buried (5); the patient was too old or too fixed in character (3); the patient was too young for other than expressive play therapy (3); the patient would be more suitably treated at a child guidance clinic (2), or the patient was unable to come for treatment for geographic reasons (6).

Brief psychotherapy only could be offered because of the nature of the unit. It was unusual for patients to attend more often than once weekly; the average number of visits was 10 over a period of three months. The approach to individual patients was dynamic and analytically oriented. Group treatment was offered to five patients. Continuation of physical treatment was unavoidable in the circumstances; yet it remained unchanged throughout the course of the psychological treatment.

Twenty-nine of the 34 patients treated benefited by psychotherapy both physically and mentally. It was possible to recall 21 patients for follow-up by a dermatologist three to 18 months after the termination of the treatment (average, 10 months). In his assessment seven of the 21 patients were greatly improved and seven had lost their eczema altogether.

An immediate complication of treatment in a few cases was an exacerbation of the eczema attributable to the bringing of unconscious conflicts into consciousness; in others psychoneurotic symptoms became manifest while the eczema subsided.

CONCLUSIONS AND COMMENTS

It has been shown that endogenous eczema is a disease which occurs in emotionally insecure individuals and that its onset and its relapses are often precipitated by situations which threaten these persons' sense of security.

This constellation, of course, is found in many individuals who nevertheless enjoy excellent health and also in many other disease states. The question may justifiably be asked why eczema patients have eczema when they do.

Constitutional predisposition has already been discussed.

Allergic predisposition undoubtedly plays a part in many cases, but it cannot be the sole etiological factor because many individuals have positive reactions to skin tests and yet eczema or allergic manifestations do not develop. Moreover, it has been shown that a latent allergic predisposition can be mobilized by

emotional factors.[2] At any rate, the demonstration of an allergic predisposition does not disprove the existence and relevance of emotional factors.

Our observations in cases of eczema tally closely with those obtained by French and Alexander for asthmatics.[3] But the questions of why one individual has asthma and another eczema and why these two conditions frequently alternate in the same individual must remain unanswered in the light of our present knowledge.

In a small number of patients the localization of the rash seemed to have a symbolic and purposeful meaning. Cases 4 and 5 gave examples of hysterical stigmatization. The hands and lips in these cases were the focus of conflictful feelings and became the site of the eczematous eruptions. Other examples include eruptions on a wedding ring finger during marital infelicity, on the manipulating finger after a guilt-ridden extramarital *affaire* and at the umbilicus after the death of the mother.

Is there a deeper significance attached to the classic distribution of eczema? The usual distribution of eczema is on the flexural surfaces of the arms and on the face. Jelliffe[4] has pointed out that the exuding skin aspires to caress or to be caressed. The skin is the organ of interpersonal contact, and contact, with its implied sense of security, has been shown to be the crucial psychodynamic need of eczematous individuals. In exhibiting his eczema the patient adopts the position of the supplicant, while the weeping of the eczema, like the weeping of a child, reenforces his appeal. These gestures serve better than words to explain his need, which may indeed date from an early period before he had words to use.

SUMMARY

The psychosomatic histories of 90 patients with disorders of the "eczema family" were compared with those of 50 controls.

Specific situations were seen to precipitate the onset or relapse of eczema: threats to life and existence, threats of loss of an outside source of support or disturbance to inner established patterns, such as blows to self esteem or conflicts over sex and aggressiveness.

A hereditary predisposition to the development of eczema and respiratory disorders existed in the group studied, particularly well marked among those who had childhood eczema.

Persons with childhood eczemas showed a high incidence of "difficult" family positions.

Eczema patients as a whole tended to have been either "unwanted" or "spoiled" children and to have been more strongly attached to one parent than to the other.

A correlation was demonstrated between the childhood environment and the transparency of the adult personality. The "spoiled" children tended to be of the "undisguised" eczema type. The "unwanted" children were more likely to adopt "disguises."

2. Markus, H., and Sahlgren, E.: Acta psychiat. et neurol. **11**:119, 1936.

3. French, T. M., and others: Psychogenic Factors in Bronchial Asthma, Psychosomatic Medicine Monograph 4, National Research Council, New York, Paul B. Hoeber, Inc., 1941.

4. Jelliffe, S. E.: Sketches in Psychosomatic Medicine, Nervous and Mental Disease Monograph 65, New York, Nervous and Mental Disease Monographs, 1939.

The basic character was that of the insecure clinging child always in need of reassurance and affection. The "disguises" adopted included "limelight seeking," "self driving" and, most commonly, "resentment."

The patient's behavior under examination and in social, occupational, sexual and marital spheres is considered in detail.

The emotional consequences of a disfiguring rash are discussed.

Attention is drawn to the unintentional psychological value of routine dermatological treatments.

Brief psychotherapy was found to be practicable on an outpatient basis and was felt to have benefited ⅔ of a small group of patients.

The universality of the eczema conflicts and personality types is noted and some speculation attempted to account for the nature of this illness.

Dr. R. M. B. MacKenna, Dermatologist in Chief, St. Bartholomew's Hospital, gave help in the preparation of this paper, and Dr. Peter Borrie, Miss I. Zaphiriou and Miss K. Roberts, R. N., assisted us.

DERMATITIS REPENS: A REPORT OF TWO CASES WITH BACTERIOLOGIC STUDIES

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DERMATITIS repens was first described in 1888 by H. Radcliffe Crocker.[1] In 1903 he drew a careful distinction between dermatitis repens and acrodermatitis continua of Hallopeau. The distinction seemed somewhat forced, and later (1930) Barber stated that dermatitis repens and acrodermatitis continua were identical diseases that could conveniently be called acrodermatitis perstans.[2] The clinical description of dermatitis repens by Crocker is worth repeating in part:

> An injury, often a trivial one, has been the exciting cause. Vesicles or bullae have appeared at the site of the injury and these have ruptured and the elevated epidermis has been thrown off, leaving a bright-red surface oozing a clear or slightly turbid fluid. The border of the denuded area is bounded by a collar of the epidermis which is raised up by subjacent fluid, clear or turbid, and is sodden and irregular. Sometimes extension takes place by the continued detachment of the epidermis by further exudation, or there may be fresh vesicles or small bullae just beyond the border which break down and add a newly denuded area to the original adjacent one.[1]

It has been abundantly demonstrated that Staphylococcus aureus is readily cultured in most cases of dermatitis repens. With the advent of chemotherapy and antibiotic therapy it was natural that the sulfonamides and penicillin should be used in such cases. Neither of the patients whose cases are described here received sulfonamides, but both had a course of penicillin injections. It is unusual to obtain a pure culture of Pseudomonas aeruginosa, but pure cultures of this organism were obtained in both our cases, probably as a result of previous therapy, particularly penicillin in case 1. In case 2 it is possible that the abundant overgrowth of Ps. aeruginosa did not allow identification of a Staphylococcus that may have been present in fewer numbers. The fact remains that these two cases of dermatitis repens failed to respond to routine antibacterial measures and were found to persist and spread because of the presence of Ps. aeruginosa. The important feature recognized in these cases is that while Ps. aeruginosa was probably not the single causative organism it assumed pathogenicity under penicillin therapy.

REPORT OF CASES

CASE 1.—S. E. W., a 49 year old white married construction engineer, was first seen by us in December 1947, at which time he gave a history of a desquamative eruption of the hands of

From the Department of Dermatology, Presbyterian Hospital, and the Vanderbilt Clinic, College of Physicians and Surgeons, Columbia University.

1. Crocker, H. R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1903.

2. Barber, H. W.: Acrodermatitis Continua Vel Perstans, Dermatitis Repens and Psoriasis Pustulosa, Brit. J. Dermat. **42**:500 (Nov.) 1930.

six months' duration. Scrapings from the hands were negative for fungi, but mycelial elements were demonstrated in scrapings from the feet. A fungus growth on culture was not obtained. A diagnosis of dermatophytosis with dermatophytid was made, and the condition cleared up in three weeks with the application of a foot paint containing iodine, thymol and salicylic acid in alcohol. Fractional roentgen ray therapy was given to the hands.

The patient was not seen again until October 1948, when he told of receiving a laceration of the sole of the right foot two months previously in the course of his occupation. Healing did not take place, and a spreading eruption developed on the right foot. His local physician treated the eruption with iodochlorhydroxyquin (vioform®) ointment, boric acid soaks and calamine lotion with phenol, but no benefit was obtained. Examination of the right foot at this time revealed a moist, exudative dermatitis involving the webs of the toes, with extension to the metatarsal area on the sole and as far as the middle of the instep on the dorsum of the foot. The skin at the edge of the affected area was sodden, macerated and white, in the form of a collarette on the dorsal surfaces and ends of the toes and along the sole of the foot (see figure). The left foot was involved similarly but less extensively. The peripheral circulation was good. Scrapings were negative for fungi, and a culture on Sabouraud's dextrose agar produced no

Dermatitis repens (case 1). Note collarette of white, sodden skin at edge of affected area.

fungus growth. Methylrosaniline chloride and a bland ointment were applied locally, and 300,000 units of procaine penicillin G in aqueous solution was given intramuscularly. In the ensuing two weeks a total of 900,000 units of penicillin was given, and the local treatment was changed to application of bacitracin ointment. Use of the latter was continued for four days without effect, and no improvement was observed.

The bacterial culture at this time showed Ps. aeruginosa. Wet dressings with streptomycin solution and dilute silver nitrate solution were of no value. On November 13 applications of peroguent® (a water-soluble ointment containing zinc peroxide, 10 per cent, calcium peroxide, 1 per cent, and cetyl pyridinium chloride, 0.2 per cent) twice daily were started. Considerable improvement was noted within two days, and by December 3 the zinc peroxide preparation alone had healed the condition entirely, except for some scaliness, which subsided in a few more days. There had been no further difficulty, to the time of writing.

CASE 2.—L. C. S., a 70 year old married Austrian-born white man, was first seen by us on March 3, 1950. He stated that during the previous Christmas season an eruption had developed between the second and third toes of the right foot.[3] A clinical diagnosis of dermatophytosis

3. While this case conforms to all previous descriptions of dermatitis repens, we were unable to elicit a history of preceding injury such as had occurred in most previously reported cases and in case 1.

was made by his local physician. The right foot received 12 fractional doses of roentgen rays, and an undecylenic acid preparation was used locally. The condition became worse while under treatment, and the left foot became similarly but much less extensively involved.

When first seen by us the condition was remarkably similar to that in case 1. The second, third and fourth interdigital webs of the right foot were wet, macerated, moist, oozing and denuded of epidermis. On the toes dorsally and on the plantar surface of the foot there was a collarette of white sodden skin with pus exuding from the loose edge. The strong, foul, pungent odor quickly permeated the entire room. The dorsalis pedis pulse was strong, but the artery had a pipe stem feel to palpation.

Scrapings for fungi failed to reveal myceliums by direct microscopic examination, and cultures on Sabouraud's dextrose medium showed no fungus growth. Culture for bacteria was made.

The clinical impression was dermatitis repens caused by a Staphylococcus. Potassium permanganate soaks (1:8,000) were prescribed, and 300,000 units of procaine penicillin in aqueous suspension was given intramuscularly daily for four days. On March 8 the patient exhibited a scaly erythematous eruption of the buttocks and a fine papular rash on the trunk that were thought to be caused by the penicillin. The feet showed less exudation at this time, and the odor was diminished, although the process was still active. The bacterial growth on culture was identified as a pure growth of Ps. aeruginosa. With case 1 in mind, application of dressings of peroguent® was begun and the right foot was bathed twice daily for ½ to one hour in 0.5 per cent acetic acid solution. Eight daily injections of dihydrostreptomycin were given. There was steadv and continuous improvement after the dihydrostreptomycin injections were stopped. The local therapy was believed to be mainly responsible for the improvement.

Twelve days after the last penicillin injection the patient manifested severe urticaria of the hands and face. This responded quickly to antihistamine drug therapy and intravenous injections of calcium gluconate.

On April 21, 1950, verrucous, fissured excrescences were curetted from the dorsa of the second, third and fourth toes. Healing of the entire condition proceeded rapidly, and the patient was entirely free of disease 10 days later.

COMMENT

Ps. aeruginosa (synonyms—Pseudomonas pyocyanea and Bacillus pyocyaneus) is a well known source of contamination of ulcers and wounds and exhibits pathogenicity in some cases of otitis externa, otitis media and purulent infections of the genitourinary and respiratory tracts. Additionally, there are reports of fatal septicemia caused by Ps. aeruginosa.

The Pseudomonas group is comprised of about 30 organisms that are gram-negative, motile rods producing a water-soluble pigment which diffuses into the culture medium. Ps. aeruginosa is a motile, aerobic, gram-negative rod, 1.5 to 3.0 by 0.5 microns, and on agar forms smooth, round, moist, glistening colonies that have a fluorescent yellowish green color. It is the only member of the Pseudomonas group which is pathogenic in man.

Stanley in a scholarly article on pyocyaneus infections gives various treatment programs that include the use of vaccines, sulfonamides, streptomycin and wet dressings of dilute acetic acid and local application of 10 per cent urethane and 1 per cent sulfanilamide or 2.2 per cent aqueous solution of β-phenoxyethyl alcohol.[4] Meleney has used 0.25 per cent parachlorophenol in a carbowax® with some success, but the very nature of its chemical structure would seem to make it a potent skin sensitizer.[5]

4. Stanley, M. M.: Bacillus Pyocyaneus Infections, Am. J. Med. **2**:253 (March) 1949; 347 (April) 1947.

5. Meleney, F. M.: Treatise on Surgical Infections, New York, Oxford University Press, 1948.

While Meleney states that he found zinc peroxide relatively ineffective in Ps. aeruginosa infections, in our cases it has proved the most reliable agent. Several authors have commented on the usefulness of streptomycin in Ps. aeruginosa infections. Frank and associates demonstrated that while most strains responded well to streptomycin in vitro, 14 per cent of the strains tested were resistant to streptomycin.[6] In case 1 local wet dressings of streptomycin were without value, and in the second case 8 daily injections of 1.0 Gm. of dihydrostreptomycin, admittedly a small dose, seemed to be of little or no benefit.

With regard to the several antibiotics, Frank and associates [6] give the following order of diminishing effectiveness in vitro:

1. Aerosporin 2. Polymyxin	very effective
3. Streptomycin	effective, but 14 per cent of strains tested were resistant
4. Aureomycin 5. Chloramphenicol (chloromycetin®)	necessary high concentrations too high to attain, even in the urine
6. Penicillin 7. Bacitracin	ineffective

The value of dilute acetic acid in the treatment of external otitis caused by Ps. aeruginosa has been stressed by Ochs.[7]

Reports by Howes, Fowler and Pichotka and Lewis show that sulfamylon® (paraaminomethylbenzenesulfonamide) is a valuable preparation in local infections caused by Ps. aeruginosa.[8] In view of this work, sulfamylon® is certainly worthy of trial in these infections, although it was not used in the cases reported here.

SUMMARY

Two cases of dermatitis repens, in which chronicity and persistence were ascribed to infection with Ps. aeruginosa, are described.

It is probable that similar cases will be seen more frequently because of the extensive use of penicillin, which allows an overgrowth of gram-negative Ps. aeruginosa.

Newer antibiotics may provide an easier solution to the problem of Pseudomonas infections. A satisfactory regimen was worked out for these two cases. Both patients showed pronounced improvement on treatment with peroguent.® Acetic acid soaks were helpful in case 2 but were not used in case 1. Small doses of streptomycin were of questionable value.

The characteristics of the Pseudomonas group of organisms are given, and other forms of therapy are discussed.

115 East Sixty-First Street (21).

6. Frank, P. F.; Wilcox, C., and Finland, M.: In Vitro Sensitivity of Bacillus Proteus and Pseudomonas Aeruginosa to 7 Antibiotics (Penicillin, Streptomycin, Bacitracin, Polymixin, Aerosporin, Aureomycin, and Chloromycetin), J. Lab. & Clin. Med. **35**:205 (Feb.) 1950.

7. Ochs, I. L.: Treatment of External Otitis: A Simple and Effective Technic, J. A. M. A. **142**:1361 (April 29) 1950.

8. Howes, E. L.: Recent Advances in Studying the Problems of Healing and Their Effect on the Treatment of Wounds and Burns, New York State J. Med. **44**:2006 (Sept. 15) 1944. Fowler, E. P., Jr.: Topical Applications to the Skin of the Ear Canal, Tr. Am. Acad. Ophth. **46**:637 (July-Aug.) 1949. Pichotka, J., and Lewis, R. B.: Prevention of Secondary Infection Due to Pseudomonas Aeruginosa in Frostbitten Tissue, Proc. Soc. Exper. Biol. & Med. **72**:127 (Oct.) 1949.

ESTROGENS BY LOCAL APPLICATION IN TREATMENT OF ACNE VULGARIS

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ACNE VULGARIS is associated with pilosebaceous irritative phenomena manifested as excessive oiliness, comedos, papules, pustules and cysts. These are aggregated wherever the sebaceous glands are most numerous: namely, on the face, chest and back. Only the adolescent type of acne is considered in this study.

Evidence that this disease is primarily an endocrine disturbance may be summarized as follows: (*a*) The usual incidence is at the time of puberty [1]; (*b*) the premenstrual flare-up of the lesions occurs when the estrogen level is lowest; (*c*) production of acne occurs in females who are given androgen; improvement follows on withdrawal of it, and recurrence is observed when it is given again [2]; (*d*) acne is not found in eunuchs, and (*e*) acne is much commoner in males.[3] These observations indicate that androgens produce pilosebaceous activity, and further work suggests an increase in the ratio of circulating androgens to estrogens as a causative factor in acne vulgaris.[4]

In a preliminary study,[5] the value of a cream containing estrogens applied locally in the management of relapsing acne vulgaris was indicated. It is the purpose of this paper to report further experience with this form of therapy.

MATERIALS AND METHODS

Ten men and 15 women whose ages ranged from 17 to 30 years were studied. These patients had the usual signs of acne vulgaris, such as oily skin, papules, comedos, pustules and cysts on the face, chest and back. The condition in these patients had proved refractory to usual methods of treatment, since all had had one or two courses of roentgen ray therapy, ultraviolet irradiation, dietary regimens and topical application of peeling and desquamating preparations. These patients appeared to be free from other disease, and none had any other manifestation of an endocrine disturbance.

George H. C. McKeown, M.D., assistant medical director of Ayerst, McKenna & Harrison, Ltd., supplied special potencies of premarin® (estrogenic substances [water soluble]) cream. This work was aided by a grant from Ayerst, McKenna & Harrison, Ltd.

1. Mintzer, I. J.: Frequency of Certain Dermatoses in High School Girls: Report on 4,700 Girls, Arch. Dermat. & Syph. **42**:475-478 (Sept.) 1940.

2. Hamilton, J. B.: Male Hormone Substance: Prime Factor in Acne, J. Clin. Endocrinol. **1**:570-592 (July) 1941.

3. Bloch, B.: Metabolism, Endocrine Glands and Skin Diseases with Special Reference to Acne Vulgaris and Xanthoma, Brit. J. Dermat. **43**:61-87 (Feb.) 1931.

4. Lawrence, C. H., and Werthessen, N. T.: The Endocrine Dyscrasia of Acne Vulgaris in Women, Endocrinology **27**:755-758 (Nov.) 1940.

5. Shapiro, I.: Estrogenic Treatment of Acne Vulgaris: A Preliminary Report, J. M. Soc. New Jersey **46**:128-129 (March) 1949.

Local application of estrogens was employed in the form of the use of premarin® cream, a preparation which contains 2.5 mg. of water-soluble conjugated estrogenic substances (equine), expressed in terms of sodium estrone sulfate per gram of vanishing cream base. The average dose was 5 mg. of the estrogenic substances applied to the locally affected areas once daily or divided into morning and evening applications, as an after-shave cream for the men and a powder base for the women. Therapy was continued for periods ranging from one to seven months, with an average of four months. The total amount of estrogenic substances applied ranged from 150 to 700 mg.

Effects of Estrogen-Containing Cream Therapy in Acne (Premarin® Cream, 2.5 Mg. per Gram)

Case No.	Patient, Age, Sex	Duration of Acne, Years	Previous Treatment	Duration of Treatment, Months	Total Amount of Estrogenic Substance, Mg.	Results
1	A. K., 18, F	4	Salves, lotions	1	150	Discontinued because of pruritus
2	M. B., 20, F	8	Alpine light, diet	3	400	Fair
3	A. D., 22, F	10	Alpine light, diet	4	500	Good
4	E. S., 36, M	13	Alpine light, diet	4	500	Good
5	M. R., 24, M	9	Alpine light, diet	4	500	Excellent
6	E. W., 17, F	5	Alpine light, diet	5	600	Excellent
7	B. L., 19, F	7	Alpine light, diet	6	650	Excellent
8	C. B., 21, F	7	Alpine light, diet	7	700	Excellent
9	L. S., 27, M	14	Alpine light, diet	4	500	Excellent
10	S. W., 17, F	4	Additional roentgen ray therapy	5	600	Excellent
11	C. J., 18, M	4	Additional roentgen ray therapy	6	650	Good
12	H. G., 23, F	10	Additional roentgen ray therapy	4	500	Good
13	S. C., 28, F	15	Additional roentgen ray therapy	4	500	Excellent
14	J. S., 29, F	15	Additional roentgen ray therapy	5	600	Excellent
15	F. S., 30, M	15	Additional roentgen ray therapy	4	500	Excellent
16	L. Z., 18, M	3	Additional roentgen ray therapy	2	400	Fair
17	J. K., 19, F	4	Additional roentgen ray therapy	1	150	Refused to use *
18	H. H., 20, M	8	Additional roentgen ray therapy	1	150	Discontinued because of flare-ups
19	M. H., 21, F	8	Additional roentgen ray therapy	2	300	Fair
20	J. C., 30, F	15	Additional roentgen ray therapy	3	400	Excellent
21	E. S., 24, F	10	Salves, ultraviolet rays	3	400	Excellent
22	C. C., 27, M	13	Salves, ultraviolet rays	3	400	Excellent
23	H. W., 29, F	15	Salves, ultraviolet rays	4	500	Excellent
24	S. C., 30, M	15	Salves, ultraviolet rays	4	500	Excellent
25	R. P., 28, M	13	Salves, ultraviolet rays	3	400	Excellent

* Personal dislike of ointments or creams. No reaction noted.

Patients were carefully followed up to determine any systemic effects of the locally applied estrogens, such as changes in the menstrual cycle, breasts and libido.

RESULTS

The results obtained with premarin® cream are tabulated. In 15 patients the results were excellent; in four they were good, and in three, fair. Three patients could not tolerate the cream because of itching, flare-ups and cosmetic disagreeableness.

Two illustrative cases are presented, one demonstrating in a young woman and the other in an older woman the beneficial effects of premarin® cream therapy in controlling the cystic infections, oiliness of skin and other manifestations of acne vulgaris.

CASE 1.—S. W. (case 10 in accompanying table), a 17 year old girl, was seen in July 1948 with a chief complaint of "pimples" on the face, cheeks and forehead of four years' duration. She had had roentgen ray treatments the year before, and after temporary improvement the eruption had relapsed. Her dietary history showed no abnormalities; her bowel habits were not unusual; her menses were regular although she had some premenstrual tension, and her breasts were normally developed. She was placed on premarin® cream therapy, sufficient cream being used to insure application of 6 mg. of estrogenic substances daily. No other therapy was administered except drainage of the pointing pustules and exclusion of iodized salt from the diet.

Improvement was noted within three weeks, and after six weeks pronounced improvement occurred. The patient noted less premenstrual tension and dragging feeling at the menses. Her skin became less oily, and fewer new infections appeared. It was decided to stop use of the estrogen cream and to replace it with a standard sulfur preparation, in order to evaluate the role which the estrogens played. There was a slow but persistent recurrence of pustules and oiliness, so that within a month the patient demanded a return to estrogen therapy. Reinstitution of premarin® cream therapy once again caused involution of the acne.

CASE 2.—J. C. (case 20 in table), a 30 year old white woman, since the age of 13 had had severe, resistant acne vulgaris which failed to improve on treatment with diet, salves, lotions and roentgen radiation. She was markedly scarred and still presented a muddy, oily complexion, with numerous deep-seated reddish cysts about her face, which repeatedly flared up before her menses and occasionally discharged a thick, yellow material.

She was placed on treatment with premarin® cream, a sufficient amount being used to insure application of 2.5 mg. of estrogenic substances three times a day for two weeks, then twice a day for two more. Subsequently, she received a maintenance dose of 2.5 mg. of estrogenic substances by local application at night.

Within two weeks she noted a decrease in the oiliness of her skin, which acquired a satiny texture; the cysts failed to flare up before her menses and gradually subsided in size. Within three months she noted a remission of her acne for the first time.

The earliest objective changes were observed after four to six weeks. These were (*a*) a decrease in the sebaceous gland activity, (*b*) a diminished number of new comedos and pustules, (*c*) involution of old lesions and (*d*) development of a supple texture and feel in the treated areas. No systemic effects of inunction of estrogenic substances were observed.

COMMENTS

Although more than 80 per cent of clinically significant cases of acne vulgaris respond to orthodox management, the occasional stubborn relapsing type should be given the benefit of therapy by local application of estrogen substances. The present report concerns a group of such cases.

Selye states that estrogens are absorbed poorly from the skin.[6] Since only 10 to 15 per cent of the estrogens are absorbed from ointments, relatively high quantities of the cream were used in this study in order to get the desired effect on the target area.[7]

6. Selye, H.: Textbook of Endocrinology, Montreal, Canada, Acta Endocrinologica, Université de Montreal, 1947, p. 31.

7. Zondek, B.: Clinical and Experimental Investigations on Genital Functions and Their Hormonal Regulation, Baltimore, Williams & Wilkins Company, 1941.

The fairly young people with acne appear to have huge surpluses of androgenic hormone, a manifestation which is not so apparent in later life.[8] This observation may explain the fact that young patients may require large doses of estrogens locally for a beneficial response.

In acne there seems to be an alteration of the estrogen-androgen ratio. It is believed that the local application of estrogenic substances helps to restore a normal balance in the skin.

CONCLUSIONS

Remissions were observed in 60 per cent of cases of acne vulgaris, previously recalcitrant to orthodox measures, after local application to the lesions of a cream containing estrogenic substances (water soluble). No harmful effects were noted after four to six months' application of estrogens.

SUMMARY

Twenty-five patients with acne vulgaris resistant to usual therapeutic measures were treated with local application of a cream containing estrogenic substances.

Within six weeks oiliness, papules and pustules had appreciably subsided in 15 of the patients. In seven other patients the response was less prompt.

A promising new therapeutic approach to resistant acne vulgaris is described.

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8. Kenigsberg, S.; Pearson, S., and McGavack, T. H.: The Excretion of 17-Ketosteroids: I. Normal Values in Relation to Age and Sex, J. Clin. Endocrinol. **9**:426-429 (May) 1949.

PALMAR PORE PATTERNS: THEIR SIGNIFICANCE IN THE ABSORPTION OF DYES

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WHEN METHYLENE blue and other dyes are introduced into the human skin by iontophoresis, the pores of the sweat ducts and the follicle openings become stained.[1] It has been postulated that the pore pattern indicates penetration of the dye into the sweat duct.[2] A similar conclusion was reached by Abramson and associates,[3] who stated [3c] that the dye was "deposited in the orifices of the sweat glands . . . (although histologic studies of this point have not been made)." On this experimental basis the theory has been advanced that the sweat glands are important avenues for the penetration of water-soluble substances into the skin. This theory contradicts experimental data indicating that the skin of the palms is only slightly permeable or completely impermeable to a number of water-soluble substances, such as dyes,[4] allergens [5] and histamine.[6] The purpose of this study

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The rapid frozen sections for this study were prepared by Dr. Herbert Mescon.

This study was made possible by a grant from the United States Public Health Service (RG330).

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1. Rein, H.: Zur Elektrophysiologie der menschlichen Haut: I. Untersuchungen über Farbstoffeinwanderung in lebende Warmblüterhaut im elektrischen Felde, Ztschr. f. Biol. **84**: 41-50 (Jan.) 1926.

2. Ichihashi, T.: Effect of Drugs on the Sweat Glands by Cataphoresis and an Effective Method for Suppression of Local Sweating: II. The Paths of Cataphoresis in the Skin and the Influence of Perspiratory Conditions on the Cataphoretic Effect, J. Orient. Med. **25**:103-104 (Dec.) 1936.

3. (*a*) Abramson, H. A., and Gorin, M. H.: Skin Reactions: IX. The Electrophoretic Demonstration of the Patent Pores of the Living Human Skin: Its Relation to the Charge of the Skin, J. Phys. Chem. **44**:1094-1102 (Dec.) 1940. (*b*) Abramson, H. A., and Gorin, M. H.: Skin Permeability, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1940, vol. 8, pp. 272-279. (*c*) Abramson, H. A., and Engel, M. G.: Skin Reactions: XII. Patterns Produced in the Skin by Electrophoresis of Dyes, Arch. Dermat. & Syph. **44**:190-200 (Aug.) 1941.

4 MacKee, G. M.; Sulzberger, M. B.; Herrmann, F., and Baer, R. L.: Histologic Studies on Percutaneous Penetration, with Special Reference to the Effect of Vehicles, J. Invest. Dermat. **6**:43-61 (Feb.) 1945.

5. Herrmann, F.: Introduction of Allergens into the Skin by Inunction with "Intraderm": I. Additional Experimental Data on the Inunction Test, Ann. Allergy **3**:431-434 (Nov.-Dec.) 1945.

6. Shelley, W. B., and Melton, F. M.: Factors Accelerating the Penetration of Histamine Through Normal Intact Human Skin, J. Invest. Dermat. **13**:61-71 (Aug.) 1949.

is to reexamine critically the question as to whether or not palmar pore patterns are sufficient evidence of absorption through sweat glands.

EXPERIMENTAL METHODS

In one series of experiments, methylene blue, eosin Y and acid fuchsin were introduced into two separate areas on the soles of freshly amputated legs, two to three hours after operation: into one area with a current density of 0.3 ma./cm. sq. for 10 minutes, and into the other with 1.5 ma./cm. sq. for 15 minutes. After the excess stain was wiped off, skin specimens were taken and frozen in dry ice® (solid carbon dioxide) and sections were made with the rapid freezing technic of Adamston and Taylor.[7] No embedding agents, fixatives or counterstains were used.

Methylene blue pore pattern on palm. *A* indicates the pattern before the scraping of the stratum corneum with a scalpel. *B* shows the absence of the pore pattern after scraping. The arrow indicates the scraped area.

In another series the following dyes were introduced in 0.5 to 1 per cent concentrations into the skin of the palms by iontophoresis [8] with a current density of 0.3 to 1 ma./cm. sq. for five to 10 minutes: methylene blue, basic fuchsin and eosin Y (positively charged) and acid fuchsin and sodium phenolsulfonphthalein (negatively charged). In a few instances concentrations and current densities were varied without noticeable change in the final results. Thirty experiments were performed on nine healthy male students.

7. Adamston, F. B., and Taylor, A. B.: The Rapid Preparation of Frozen Tissue Section, Stain Technol. **23**:109-116 (July) 1948.

8. Shelley, W. B.; Horvath, P. N.; Weidman, F. D., and Pillsbury, D. M.: Experimental Miliaria in Man: I. Production of Sweat Retention Anidrosis and Vesicles by Means of Iontophoresis, J. Invest. Dermat. **11**:275-291 (Oct.) 1948.

RESULTS

Methylene Blue.—In agreement with Abramson's observations, pore patterns were regularly produced with methylene blue; however, the dye did not penetrate beyond the superficial layers of the stratum corneum. This last point was demonstrated in two ways: (*a*) The pore pattern was readily erased by the scraping off of the horny layer with a scalpel. This procedure may be facilitated by treatment of the skin with 10 per cent sodium hydroxide solution (figure). (*b*) Histological sections from the soles of amputated legs exhibited the dye only in the upper layers of the stratum corneum.

Eosin Y and Basic Fuchsin.—In spite of prolonged iontophoresis, no pore patterns were obtained with eosin Y and basic fuchsin. No evidence of penetration of eosin beyond the stratum corneum of the sole of an amputated foot was demonstrable.

Acid Fuchsin and Sodium Phenolsulfonphthalein.—Both acid fuchsin and sodium phenolsulfonphthalein caused consistent pore patterns which could not be removed by scraping. When acid fuchsin was introduced into the sole of an amputated foot, histological sections demonstrated no staining beyond the stratum corneum.

COMMENTS

These experiments do not support the theory that palmar pore patterns indicate penetration of a dye into the sweat gland. With methylene blue, the only dye previously used to produce palmar pore patterns, the resulting pore patterns were confined to the upper horny layer. Only acid dyes appeared to penetrate into the ducts of the sweat glands, although in the case of acid fuchsin no histological evidence of penetration could be obtained.

The disappearance of methylene blue in the deeper layers of the stratum corneum cannot be explained on the basis of its reduction to the colorless leuko form because it has been shown that only active sweat glands are capable of such activity.[9] The dead horny layer would not be able to perform such a conversion.

Our experiments on surviving skin were carried out within two to three hours after death. It has been demonstrated that during this period the permeability of the human skin remains constant.[10] Nevertheless, lack of staining in the autopsy specimens cannot be accepted as definite proof for lack of penetration. In the case of methylene blue, the penetration of the dye into the upper part of the horny layer is of sufficient intensity to become visible under the microscope. It is therefore reasonable to assume that the lower portion of the stratum corneum does not stain because of insufficient penetration of the dye into this layer. On the other hand, the possibility cannot be ruled out that acid fuchsin actually penetrates into the deeper layers of the epidermis but in concentrations not sufficiently high to become microscopically visible.

It is of interest that negatively charged dyes apparently penetrated more deeply than did the positively charged dyes. As a general rule, it is more difficult to

9. Sperling, F., and Koppanyi, T.: Histophysiologic Studies on Sweating, Am. J. Anat. **84**:335-364 (May) 1949.

10. Rein, H.: Experimentelle Studien über Elektroendosomose an überlebender menschlicher Haut, Ztschr. f. Biol. **81**:125-140 (June) 1924.

introduce anions than to introduce cations into the skin by iontophoresis, because of the opposing electroendosmotic force. Further work will be necessary to explain the anomalous behavior of the sweat ducts.

SUMMARY

The positively charged dyes methylene blue, basic fuchsin and eosin Y and the negatively charged acid fuchsin and sodium phenolsulfonphthalein were introduced into the palms of healthy persons by means of iontophoresis. Pore patterns could be obtained with methylene blue, acid fuchsin and sodium phenolsulfonphthalein. The pore pattern caused by methylene blue could be erased by the scraping of the skin surface, while the pore patterns obtained with the negatively charged dyes could not be abolished completely by this method. Histological sections taken from the soles of amputated legs revealed no penetration of the dyes into the skin. Although these observations do not disprove penetration through the sweat glands, they indicate that palmar pore patterns are insufficient evidence for this form of percutaneous penetration.

TELANGIECTASIA MACULARIS ERUPTIVA PERSTANS

Review of the Literature, Report of a Case and Discussion of the Etiology and Pathology of Generalized Telangiectasia

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IN REPORTING on a slide sent to him for an opinion as to the diagnosis in the case to be presented here, one of the leading dermatologic histopathologists in this country made this comment, "The series of words 'telangiectasia macularis eruptiva perstans' fits the picture; however, I am unacquainted with any such disease." A search through a number of better known textbooks of dermatology revealed only two references to it. Andrews,[1] in describing urticaria pigmentosa, stated briefly, "Persistent red macules with scarcely any pigmentation are observed in some cases. To these, Weber, Barber, and others have given the name telangiectasia macularis eruptiva perstans." Sutton and Sutton [2] devoted a brief but comprehensive paragraph to the disorder and agreed to its interrelation with urticaria pigmentosa. It appears that a review of the literature on this subject and a report of a case is therefore justified.

In 1930 Parkes Weber and R. Hellenschmied [3] described a rare case, of Mrs. F. N., a 60 year old somewhat obese woman who for at least 20 years had had an eruption which was characterized by persistent round discrete or confluent red macules 2 to 6 mm. in diameter, most of which were not elevated, although a few projected very slightly above the general level of the skin. They faded completely under diascopic pressure, leaving only a faint brownish pigmentation in some of them. They were distributed chiefly over the upper part of the front of the thorax, the outer surfaces of the upper extremities and on the abdomen. The face was free from the macules but presented many linear or arborescent telangiectases of the ordinary kind. There were no purpuric lesions

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Colonel Moursund and Colonel Hirschmann are Senior Resident and Resident, respectively, in Dermatology and Syphilology.

1. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 690.

2. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 175.

3. Weber, F. P., and Hellenschmied, R.: Telangiectasia Macularis Eruptiva Perstans, Brit. J. Dermat. & Syph. **42**:374 (Aug.-Sept.) 1930.

anywhere. There was no evidence to suggest a neuropathic or a traumatic causation. The possibility of a toxic origin was considered. No evidence of hepatic disease was found. The patient had a duodenal ulcer and mild hypertension, but no relation between these conditions and the eruption could be made out. Weber and Hellenschmied [3] termed this condition "telangiectasia macularis eruptiva perstans." In designating the red macules "telangiectatic," they explained that they used the word in its exact sense to signify persistent dilatation of the terminal blood vessels, whether the individual dilated blood vessels could be distinguished by ordinary inspection with the naked eye or not.

Later in the same year, Parkes Weber,[3] in studying a typical case of urticaria pigmentosa in a 26 year old woman, found that the patient had some red macules also which faded on diascopic pressure, leaving slight brownish pigmentation, and which became increasingly red and elevated on being rubbed. On reexamining Mrs. F. N., he found that her macules became increasingly red and elevated on being rubbed and that she exhibited slight factitious urticaria over the back of the thorax. Recognizing the possible relation between these two conditions, Weber made the observation that "telangiectasia macularis eruptiva perstans may turn out to be allied to—that is to say, a very rare telangiectatic, relatively pigmentless variety of urticaria pigmentosa of adults in more elderly subjects."

In 1935 Weber and Rast [4] stated that the most characteristic cases of this relatively rare condition of macular telangiectasia occur in rather fat middle-aged women. Individual dilated capillaries usually cannot be seen in connection with the red macules though there may be well marked ordinary linear or arborescent telangiectases on the face, which is usually free from obvious macules. The macular eruption may appear at any age though usually in adult life. When once present, never, so it seems, does the eruption disappear. Purpuric lesions of all kinds are absent. Though the condition is supposed to occur more characteristically in fat, middle-aged women, our case and four previously reported cases under this title occurred in men—two middle aged and two elderly. Brocq,[5] who reported his observations of this condition in 1921, though calling it *"telangiectasies essentielles en plaques acquisés,"* stated that it was not confined to adults or to obese women but occurred at any age, the lesions usually appearing on the limbs and later scattering over the trunk, the face rarely being affected. He described the individual lesions as varying in size from that of a pinhead to that of a dime and their surface as being slightly powdery or atrophic. Ball,[6] who reported

4. Weber, F. P., and Rast, H.: Telangiectasia Macularis Eruptiva Perstans, Acta dermat.-venereol. **26**:216, 1935.

5. Brocq, L.: Précis-atlas de practique dermatologique, Paris, Gaston Doin, 1921, p. 1043; cited by Weber and Rast,[4] p. 217.

6. Ball, F. I.: Telangiectasia Macularis Eruptiva Perstans, Arch. Dermat. & Syph. **36**:65 (July) 1937.

a case of eruptive telangiectatic macules in a 10 year old obese girl in which spontaneous healing occurred, proposed that the term "perstans" be omitted from the designation of this condition.

A more or less generalized eruption of persistent red or purple telangiectatic macules in adults apparently is of considerable rarity, though a form, generally in fat women, has for a long time been recognized in France. Weber and Hellenschmied [3] in their original article pointed out that most of the cases from the literature which can be included under the designation telangiectasia macularis eruptiva perstans have been referred to in S. W. Becker's comprehensive monograph on "Generalized Telangiectasia." [7] It included the remarkable eruptive macular series extracted, mostly from earlier French records, by T. Colcott Fox [8] under the subheading "essential telangiectases en plaques." Such cases were described by Levi as *"telangiectasies acquisées généraliésees"* and by Brocq [5] as *"telangiectasies essentielles en plaques acquisés."*

Reports recorded in France by E. Vidal [9] as early as 1880 and by others included cases which undoubtedly were of this same condition. Vidal's case was that of a neuropathic 31 year old woman who had urticaria at the onset of menstruation. Shortly thereafter, she began to acquire permanent red macules on the inside of the forearms, and the eruption gradually extended to the breast, neck, wrist, backs of the hands, the lumbar and dorsal regions, the belly, the internal aspects of the thighs and the soles. The lesions were lenticular, slightly raised and, on the forearms, confluent. The patient had pruritus and was dermographic.

Sir William Osler in 1907 described a case of "telangiectasis circumscripta universalis" [10] which may be included in this series. The patient was a 39 year old man whose skin presented a remarkable appearance. Large portions of his trunk and extremities were sprinkled more or less closely with dark red macules, varying from 2 to 6 mm. in diameter. They were thickly set over the chest and back and on the flexor surfaces of the forearms and inner aspects of the arms. Under pressure they disappeared, leaving only a slight brownish tinge. They were, therefore, not purpuric but telangiectatic, although by simple inspection no individual blood vessels could be distinguished. Their ordinarily dark purplish color could be changed to a vivid red by rubbing, and they were not raised above the general level of the skin. Factitious urticaria could

7. Becker, S. W.: Generalized Telangiectasia: Clinical Study, with Special Consideration of Etiology and Pathology, Arch. Dermat. & Syph. **14**:387 (Oct.) 1926; cited by Weber and Hellenschmied,[3] p. 380.

8. Fox, T. C.: A Case of Bilateral Telangiectases of the Trunk, with a History of Marked Epistaxis in Childhood and Recent Rectal Haemorrhage, Brit. J. Dermat. **20**:145 (May) 1908.

9. Vidal, E.: Télangiectasia accidentelle, symetrique et généralisée, Bull. et mém. Soc. méd. d. hôp. de Paris **17**:186, 1880; cited by Weber and Rast,[4] p. 217.

10. Osler, W.: Telangiectasia Circumscripta Universalis, Johns Hopkins Hosp. Bull. **18**:401, 1907; cited by Weber and Rast,[4] p. 218.

be readily produced. Since the macules were of 10 years' duration, they could be called permanent. During that time, although they had never disappeared, they had been less intense in color during the summer than during the winter.

In their paper of 1935 Weber and Rast [4] described 11 cases, including three of their own, which seem to meet the criteria of and fall into the category of telangiectasia macularis eruptiva perstans. In this series of cases the only mention of subjective symptoms was that itching is not prominent, although one patient complained of moderate generalized itching and another patient had slight itching after a long walk or on rubbing the skin.

Likewise, little mention is made of treatment except that no satisfactory treatment is known. There are frequently accompanying features which require treatment by diet or otherwise. Calcium therapy failed in one case. Reduction of alcohol intake improved the condition in one case.

It was found that, as in typical urticaria pigmentosa of adults, mast cells may or may not be present in the lesions of this condition. Two cases of the 11 showed mast cells. Weber suggested that the presence or absence of mast cells may depend on the stage in the evolution of the lesion examined.

A biopsy report by Dr. I. Muende in one of Weber and Rast's [4] cases described a pronounced edema of the pars reticularis and papillaris with dilatation of the papillae, a decided dilatation of the blood capillaries and lymphatic spaces, a considerable hyperplasia of endothelial cells with a few giant cells around a hair follicle, a very dense small round cell infiltration in the upper part of the corium, no excessive pigment and no mast cells. In another case Dr. Muende described a slight hyperkeratosis associated with hypertrophy of the stratum granulosum, a flattening of the epidermodermal junction, pronounced pigmentation of the stratum germinativum in places, a slight perivascular small round cell infiltration, an excess of cells of a young fibroblastic type between the collagen bundles and extending throughout the entire thickness of the corium and no distinct mast cells.

REPORT OF CASE

A 46 year old white man, register no. 406312, was admitted to Brooke General Hospital on Nov. 19, 1946, with a transfer diagnosis of poikiloderma atrophicans vasculare (Jacobi). His chief complaint was a generalized eruption with severe, almost constant, itching which was made worse when he became overheated by exercise or by hot weather.

His past history revealed that he had had the usual childhood diseases, a tonsillectomy in 1927, right nephrolithiasis in 1933, acute, suppurative and bilateral pyelonephritis in 1933, influenza in 1934, bronchitis in 1937 and a reaction from tetanus toxoid in 1941. A review of military records revealed a diagnosis of urticaria pigmentosa made at the Station Hospital, Fort Sam Houston, Texas, on Aug. 22, 1941, and a macular rash of the trunk and extremities had been noted on physical examination on April 6, 1942. There was no history of allergy in the patient or in his family.

According to the patient, the present illness began during an influenza epidemic in January 1946 in Washington, D. C., when, after having been vaccinated with influenza vaccine, he acquired influenza which lasted for about eight days, during which time he had fever, cough, diarrhea, vomiting and general aching. He was given sulfadiazine for three or four days, and then, because of the onset of a rash which began first in the groin, he was hospitalized for 13 days. During

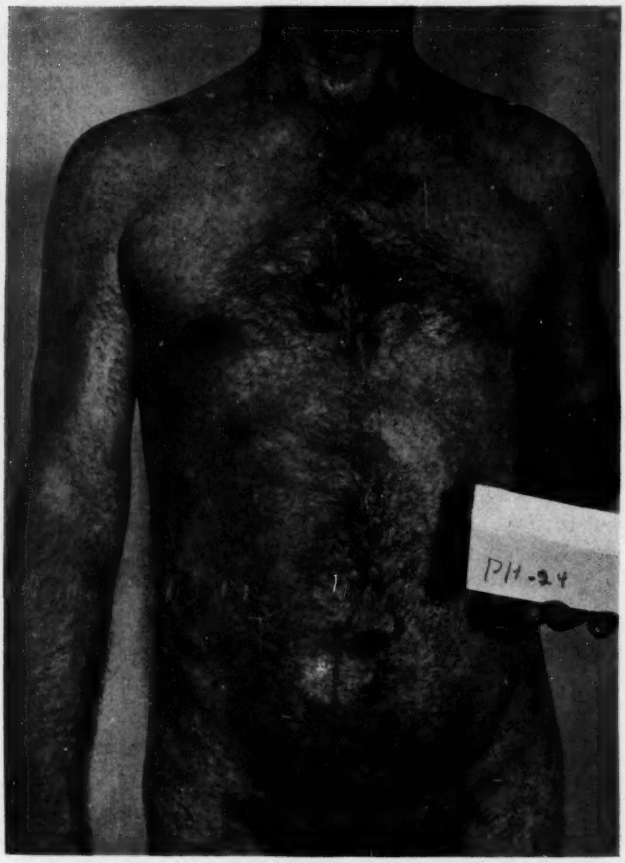

Fig. 1.—Diffuse and almost confluent but discrete macular eruption involving trunk and upper extremities (Brooke General Hospital, United States Army, negative no. 24, June 19, 1947).

this time he had gross hematuria which was considered to be the consequence of the sulfadiazine therapy and he was told that he had uremia. No particular notice was taken of his eruption, but, after being discharged from the hospital early in February 1946, he was given ultraviolet irradiation for the eruption with no beneficial results; in fact, the eruption extended, particularly over his back and arms. Otherwise he felt well.

The patient went to Korea in May 1946. During the next three months the eruption continued to spread until almost the entire body was involved. In June 1946 he began to have pains in the lower extremities, especially in the hip and knee joints and in the muscles, with occasional muscle cramps. He became fatigued easily, had little appetite, noted some shortness of breath and occasionally noted burning on urination. In view of the eruption and the associated symptoms

Fig. 2.—Factitial urticaria produced by stroking of the skin with the finger nail (Brooke General Hospital, United States Army, negative no. 23, June 19, 1947).

he was hospitalized in Korea in July 1946, was returned to the United States as a patient and admitted to an Army general hospital, where his eruption was considered to be poikiloderma atrophicans vasculare (Jacobi). The additional symptoms had subsided by this time.

For administrative reasons the patient was transferred to Brooke General Hospital. The physical examination revealed a generalized more or less symmetric macular eruption which spared only the face, scalp, palms and soles and

small areas on the flexor surface of the forearms and legs. There was only slight involvement of the backs of the hands and the neck but diffuse, almost generalized involvement of the entire trunk, the arms and the thighs, especially on the upper part of the back, in the axillas, in the flanks, in the groins, on the outer surface of the arms and on the thighs (fig. 1). The eruption consisted of small discrete or confluent reddish brown and faint brown macules ranging from the size of a pinhead to that of a pea, with considerable tendency to coalesce in the more profuse areas of involvement. The faint brown macules seemed to be simply brownish pigmentation. The reddish brown macules faded on diascopic pressure, completely in some instances but leaving a faint brownish pigmentation in others. A slight amount of fine scaling was noted in the involved areas. No purpuric lesions were seen. No atrophy could be made out, although previous examiners thought that there was a slight amount of atrophy in some areas. Urticarial wheals and ridges could be produced by stroking of the skin (fig. 2). No evidence of depigmentation could be seen. In addition, the patient had a mild seborrheic dermatitis. There was moderate telangiectasia of the ordinary type involving the skin of the nose and cheeks. No involvement of the mucous membranes was seen. There was palpable nontender lymphadenopathy of the cervical and axillary lymph glands. The blood pressure was 135 systolic and 88 diastolic. The patient was slightly obese. Otherwise, physical examination revealed an essentially normal condition. Results of routine laboratory tests, including complete blood count and urinalyses, were within normal limits. The bleeding time was 1 minute, 45 seconds; the clotting time was 2 minutes, 35 seconds; the platelet count was 415,000; and the prothrombin time was 21 minutes. The Kahn reaction of the blood was negative. The feces were negative for ova and parasites. The values for blood cholesterol, urea nitrogen, uric acid, creatinine, phosphorus and calcium and the icterus index were all normal. The result of the glucose tolerance test was normal. The blood total protein was 7.8 Gm. per hundred cubic centimeters with 5.1 Gm. of albumin, 2.7 Gm. of globulin and an albumin-globulin ratio of 1.9; the ketosteroids in the urine were 16.4 mg. in 24 hours as androsterone. The basal metabolic rate was normal. Roentgenograms of the lungs and skull revealed no abnormality. The roentgenogram of the heart revealed it to be within normal limits. The electrocardiogram suggested possible left ventricular preponderance; otherwise it was normal.

Dental, eye, ear, nose and throat, genitourinary and medical consultations revealed nothing of significance. An allergy survey revealed no specific sensitivities; however, only routine intradermal tests with foods and inhalants were done.

A cutaneous biopsy stained with hematoxylin and eosin revealed a connective tissue type cell infiltrate, chiefly in the upper part of the cutis, including the papillary bodies and in columns and strands between collagen fibers and about the blood vessels. There was also slight round cell perivascular infiltration. Melanin pigmentation in the basal cell layer of the epidermis was increased focally. Chromatophores were present in moderate numbers. There was no atrophy of the epidermis or cutis. There was moderate edema of the cutis but little if any edema of the epidermis. No hemorrhage or hemosiderin pigment was seen in the section (fig. 3). This picture ruled out poikiloderma atrophicans vasculare and, in retrospect, suggests that of urticaria pigmentosa except that no mast cells were recognized with the hematoxylin and eosin stain. A slide was sent to a civilian consultant of the Army Institute of Pathology, whose opinion was as follows: "The disease was extremely superficial and only slightly inflammatory, the condition being such as might be seen in tinea versicolor or perhaps tinea nigra, but no fungi could be found. It was possibly due to arsenicals or was only a freckling condition. Poikiloderma atrophicans vasculare was excluded. The series of words 'telangiectasia macularis eruptiva perstans' fit the picture; however, I am unacquainted with any such disease." (The consultant did not have the benefit of a polychrome methylene blue–stained slide). The idea that the patient had urticaria pigmentosa persisted, and later, on carefully examining another

slide of the case, Col. Elbert De Coursey, chief of the laboratory service, Brooke General Hospital, found several cells which suggested mast cells. Additional sections were stained with polychrome methylene blue, and numerous mast cells were demonstrated (fig. 4). The prussian blue stain showed an absence of iron pigment in the lesion.

Some question might be raised concerning the failure to demonstrate telangiectasia histologically in this case and the use of the term "telangiectasia" in the diagnosis of this condition. It will be recalled that Weber and Hellenschmied [8] in their original description of this disease stated that in designating the red

Fig. 3.—Infiltrate, chiefly in the upper part of the cutis, including papillary bodies and in columns and strands between collagen fibers and about the blood vessels with a slight round cell perivascular infiltration; focal increased melanin pigmentation in basal cell layer; numerous chromatophores in the cutis; hematoxylin and eosin, × 200 (Brooke General Hospital, United States Army, negative no. 205, Aug. 13, 1947).

macules "telangiectatic" they used the word in its exact sense to signify persistent dilatation of the terminal blood vessels, whether the individual dilated blood vessels could be distinguished by ordinary inspection with the naked eye or not. There were no grossly visible telangiectatic vessels among the typical lesions in our case, but certainly there were papillary ectasias or circumscribed red macules which faded on diascopic pressure. Secondly, it will be recalled that in one of the two cases examined histologically by Dr. I. Muende no mention was made of dilatation of the capillaries. It is possible and even probable that if another

biopsy had been taken in that case as well as in ours telangiectasia would have been demonstrated histologically. Apparently the histologic demonstration of telangiectasia is not necessary in the diagnosis of this disease.

The faint brown macules and the faint brown pigmentation which remained on diascopic pressure of the red macules can probably be explained by the focally increased melanin pigmentation in the basal cell layer. The explanation of this focally increased pigmentation remains obscure.

In making the final diagnosis for this patient, two other possible diseases had to be considered. The patient had had a toxic reaction to sulfadiazine in 1946, just prior to the rapid progression of his eruption. Shortly thereafter, ultraviolet

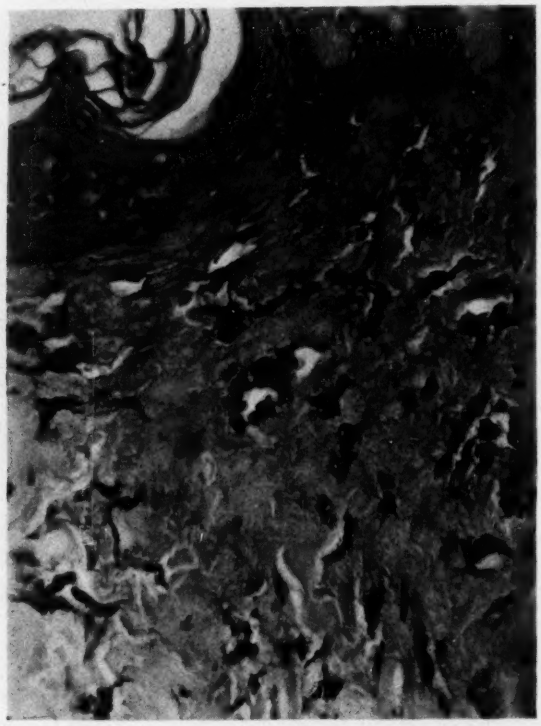

Fig. 4.—Mast cells in cutis; polychrome methylene blue, × 450 (Brooke General Hospital, United States Army, negative no. 1441-1, June 8, 1948).

irradiation was used and the eruption seemed to spread even more rapidly. The possibility of a persistent drug eruption with an associated sensitivity to light had to be considered. No report of such an occurrence from reaction to sulfadiazine could be found in the literature, but probably that possibility still has to be retained. In June 1946 the patient, in addition to widespread involvement of his skin by the eruption, began to have pains in the lower extremities with occasional muscle cramps, fatigue and anorexia. This occurrence suggested the possibility of poikilodermatomyositis. Since these additional symptoms subsided completely and no muscle tenderness, weakness or atrophy could be found on physical examination and since the clinical and histologic picture was not that of poikiloderma, it was

believed that this disease could be ruled out. So, with the histologic picture and the history and clinical picture previously described, it is believed that this case represents a typical example of telangiectasia macularis eruptiva perstans.

Throughout his period of observation the patient's dermatosis continued unchanged. He was fairly comfortable when cool but had an urticarial reaction and itched severely when overheated. A thorough survey of his case revealed no specific cause for his disabling skin condition; therefore, no specific therapy was used. Some relief from the pruritus was afforded by the use of diphenhydramine (benadryl®) hydrochloride in a dosage of 50 mg. in the morning and in the afternoon and 100 mg. at bedtime.

COMMENTS

The term "telangiectasia macularis eruptiva perstans" is simply an objective designation and does not connote anything about the systemic background. Even "adult urticaria pigmentosa," for which it is a synonym, does not assist materially in the classification or explanation of this disease condition. Still, no better designation seems to be immediately available. Perhaps a differential diagnosis of the disease, a brief review of the literature on the subject of the etiology, pathology and classification of generalized telangiectasia and some speculation as to the causation and pathogenesis in this particular case will assist in the finding of a place for this disease.

In the way of differential diagnosis, the clinical and histologic features of the more important diseases to be considered are given in the accompanying table.

Turning to the etiology of generalized telangiectasia, we find that apparently it was relatively easy for the earlier reported cases to fall into an idiopathic or essential category. Even now this situation seems to exist and is probably the result of incomplete study of the cases. The possibility of a neuropathic or a traumatic etiology was considered by some of the earlier authors, and most of them pointed out associated disease conditions but did not link them with the generalized telangiectasia. Apparently Lanceplaine,[11] in 1904, was the first to attempt to classify the essential telangiectasias etiologically. He divided them into three groups—neurogenous, mechanical and toxic. Then, in 1908, Colcott Fox [8] classified the telangiectasias as follows: (1) nevi, under which he grouped angioma serpiginosum; (2) Majocchi's disease; (3) telangiectases complicating various dermatoses; (4) telangiectases symptomatic of disturbances of the general circulation (limited practically to Osler's syndrome), and (5) essential or primary telangiectases, under which category he included senile angiomas of Dubreuille. It remained for Stokes [12] in 1915 to analyze thoroughly the then reported cases of essential generalized telangiectasia and to advance some really constructive theories as to the causation of at least some of these cases. From study of a case of generalized telangiectasia in association with

11. Lanceplaine, R.: Étude sur les télangiectasies essentielles, Thesis, Paris, no. 236, Paris, 1904; cited by Becker,[7] p. 408.

12. Stokes, J. H.: Generalized Telangiectasia in Association with Syphilis, with the Pathological Picture of Peripheral Vascular Sclerosis, Am. J. M. Sc. **149**:669 (May) 1915.

syphilis and from reviewing the literature, Stokes [12] came to the conclusion that well known factors in cardiovascular pathology such as syphilis, chronic plumbism, hyperthyroidism and nephritis may be suspected of forming the etiologic background for the cutaneous mani-

Differential Diagnosis of Telangiectasia Macularis Eruptiva Perstans

	Telangiectasia Macularis Eruptiva Perstans (F. P. Weber)	Poikiloderma Atrophicans Vasculare (Jacobi)	Purpura Annularis Telangiectodes (Majocchi)	A Peculiar Progressive Pigmentary Disease of the Skin (Schamberg's Disease)	Angioma Serpiginosum (Hutchinson)	Pigmented Purpuric Lichenoid Dermatitis (Gougerot and Blum)
Clinical	Discrete or confluent red-brown macules and pigmentation on the trunk and extremities. Macules fade on diascopy and become increasingly red and elevated when rubbed. Pronounced dermographism. No atrophy. No purpura. Severe pruritus on exposure to heat or exercise. Persistent.	Widespread to universal healed radiodermatitis-like eruption with gross telangiectasia, pigmentation, atrophy and hemorrhages. Telangiectasia and leukoplakia-like lesions in mouth. May be moderate itching. Persistent.	Minute red puncta to annular, telangiectatic, purpuric, pigmentary and atrophic lesions, usually occurring on the legs. Usually clears up after several months, leaving slight atrophy and achromia. No symptoms.	Progressive development of patches of small reddish puncta "grains of cayenne pepper," and brown to brownish yellow pigmentation of ankles, shins, dorsa of feet, knees and flexor aspects of wrists. Asymptomatic.	Grouped minute copper to bright red puncta with peripheral extension to form circinate and serpiginous lesions with clear centers. Eruption predominates on lower extremities but may be generalized. Little if any pigmentation. No purpura. Symptoms slight. Persistent.	Discrete and grouped 0.25 to 2 mm. pink to orange-red purpuric or telangiectatic slightly elevated papules occurring most commonly on lower extremities. May occur on upper extremities and trunk. Lesions may be pigmented in varying shades. Pruritus variable. May last for years.
Pathologic	Slight perivascular lymphocytic infiltration and slight to moderate connective tissue type cell infiltrate, chiefly in upper part of cutis, including papillary bodies and in columns and strands between collagen fibers and about blood vessels. Focal increased melanin pigmentation in basal cell layer. Moderate edema of cutis; little if any of epidermis. Moderate number of chromatophores in cutis. No atrophy, hemorrhage or hemosiderin pigment. Telangiectasia variable. Numerous mast cells demonstrated by polychrome methylene blue stain.	Moderate perivascular lymphocytic infiltration in upper part of cutis and papillary bodies. Moderate edema of cutis and pronounced intercellular edema of basal and adjacent cells. Numerous chromatophores in cutis. Atrophy of epidermis, elastic and collagenous tissues prominent. Hemorrhage may be seen. Pronounced telangiectasia of capillaries in upper part of cutis. A few mast cells may be seen.	Moderate perivascular lymphocytic infiltration. Moderate edema of cutis. Hemorrhagic areas with deposits of hemosiderin pigment. Late atrophy of epidermis. Dilated capillaries and lymph spaces. Phlebitis and obliterating endarteritis. Degenerative changes in hair follicles, coil and sebaceous glands and nonstriated muscle.	Dense lymphoid, polymorphonuclear and epithelioid cell infiltrate in papillary and subpapillary layers, particularly about sweat ducts. Moderate edema of cutis. No hemorrhages, but hemosiderin pigment, intracellular and free in tissues, can be demonstrated. May be atrophy of epidermis. Telangiectasia of capillaries and lymph spaces is seen. A few mast cells may be seen.	Moderate perivascular lymphocytic infiltration of the papillary and subpapillary layers. Mild intracellular and intercellular edema of prickle cell layer and moderate liquefaction degeneration of the basal cell layer. No hemorrhage or hemosiderin pigment. Alternate atrophy and mild acanthosis of epidermis. Definite telangiectasia and capillary proliferation. Slight degeneration of collagen fibers.	Moderate perivascular lymphocytic and plasma cell infiltrate. Hyperkeratosis and parakeratosis. Rete malpighii thinned and edematous, and granular layer practically absent. Free red blood cells in infiltrate and intracellular and extracellular iron pigment granules. Vessel walls edematous. Some endarteritis.

festations of at least a portion of the so-called primary idiopathic or essential cases of generalized telangiectasia. Both the clinical and the pathologic studies of these cases strongly supported this theory. In 1926, Becker,[13] in another complete review of the literature, came to the

13. Becker, S. W.: Generalized Telangiectasia: A Clinical Study, with Special Consideration of Etiology and Pathology, Arch. Dermat. & Syph. **14**:387 (Oct.) 1926.

conclusion that the essential or idiopathic generalized telangiectasias may be divided etiologically into four types—infectious, endocrinous, cardiovascular and neurogenous—these four types admittedly being interdependent. He left it for later observers to break down these types further into unique groups with a common etiology. From his remarkable table 1, which outlined the salient etiologic and pathologic features of 68 cases of generalized telangiectasia previously reported and reported by him, one may conclude as follows: 1. Females are affected more than twice as frequently as males, and in these females, endocrine and neurogenous factors are prominent. 2. The dermatosis appears more often in the second decade. 3. Among the associated infections reported, syphilis was outstanding and was diagnosed or suspected in 21 of the cases. 4. Among the endocrine disturbances, obesity was most prominent, with puberty, hyperthyroidism or goiter, the menopause and diabetes following closely. 5. Among the associated cardiovascular and renal disturbances reported, myocarditis, nephritis and arteriosclerosis were most frequently mentioned. 6. Among the disturbances of the nervous system, Becker included urticaria and dermographism, which were of outstanding frequency, with the trite "nervousness" following closely. 7. Finally, in most of the cases there was a multiplicity of these associated conditions, and it may be this bombardment of the vasomotor mechanism simultaneously from multiple directions which is accountable for the picture that is presented in the skin. As stated by Becker,[13] "the rarity of generalized telangiectasia and the banality of the presumably causal conditions suggest an inherent predisposition."

Trawinski [14] cited Majocchi as advancing an angioneurotic hypothesis and a theory of direct action by some toxin on the vessels themselves in purpura annularis telangiectodes. Stokes [12] stated that, according to this view, cardiac disease, syphilis and infectious diseases or any toxin or toxin-producing agent which can excite endothelial reaction and proliferation may serve as the basis for Majocchi's syndrome, and the acceptance of such a view would seem to include purpura annularis telangiectodes in the etiologic classification shared by cases of generalized telangiectasia of the essential type. It would seem, then, that we must give Majocchi credit for first suggesting an allergic etiology for generalized telangiectasia.

Speculating now on the causation and pathogenesis of our case, we must recall several seemingly pertinent events in the history. First, we must assume that the patient was truthful in stating that he had had no similar eruption prior to 1941, at which time he was 41 years of age, because in the usual case of urticaria pigmentosa developing in childhood the disease persists even after long periods. It would seem that the patient's repeated and frequent exposure to physical examinations as a soldier without any reference in his records to an eruption until 1941 would lend weight to his statement. Of course, we still cannot definitely

14. Trawinski, H.: Monatshefte f. prakt. Dermat. **1**:45, 1910; cited by Stokes,[12] p. 694.

rule out ordinary urticaria pigmentosa because many instances are recorded of its development only in adult life. Next we find that in August 1941 the patient had an eruption following a reaction to tetanus toxoid immunization, and, although he stated that this eruption was different from the one he later acquired, he was diagnosed as having urticaria pigmentosa at Station Hospital, Fort Sam Houston, Texas, on Aug. 22, 1941. Finally, we find in his history that in January 1946 he acquired influenza (reaction?) after vaccination with influenza vaccine, after which development his eruption slowly but progressively became more prominent and more generalized. From these facts we find that there is a suggestion of some toxic or allergic agent involved in the production of his eruption. The fact that the patient secured some relief from his pruritus from medication with diphenhydramine (benadryl®) may even be of some significance.

Reference to a few articles in the literature would seem to lend further weight to the theory that the tetanus toxoid reaction played at least some part in the development of the eruption. In 1940 Cooke [15] reported on allergy induced by immunization with tetanus toxoid, and in the same year Whittingham [16] and Cunningham [17] reported on anaphylaxis following administration of tetanus toxoid. In 1942 Sulzberger [18] reported a case of chronic urticaria of over six months' duration which began three days after an initial injection of tetanus toxoid. Long [19] in summing up the subject of tetanus in the United States Army in World War II discussed the reactions to tetanus toxoid and stated that, although the frequency of reactions was relatively low, an occasional person would manifest an early appearance, usually 30 minutes after injection, of flushing and itching of the skin or of frank urticaria or angioneurotic edema. The majority of reactions occurred early in the tetanus immunization program and were recognized as manifestations of sensitivity to some constituent of the toxoid used. About 85 per cent of reactions of this type occurred after the second or third dose, suggesting the production of a hypersensitive state by the previous dose rather than a preexisting sensitivity. This observation, considered in the light of the experience of Cooke [15] and Whittingham [16] and associates with the sensitizing properties of Witte's and Berna's peptones in toxoids, led to cessation of the use of toxoids containing these peptones with a resultant much lower rate of reactions to tetanus toxoid. In the

15. Cooke, R. A.; Hampton, S.; Sherman, W. B., and Stull, A.: Allergy Induced by Immunization with Tetanus Toxoid, J. A. M. A. **114**:1854 (May 11) 1940.

16. Whittingham, H. E.: Anaphylaxis Following Administration of Tetanus Toxoid, Brit. M. J. **1**:292 (Feb. 24) 1940.

17. Cunningham, A. A.: Anaphylaxis After Injection of Tetanus Toxoid, Brit. M. J. **2**:522 (Oct. 19) 1940.

18. Sulzberger, M. B.: Chronic Urticaria Following a Single Injection of Tetanus Toxoid, U. S. Nav. M. Bull. **40**:415 (April) 1942.

19. Long, A. P., and Sartwell, P. E.: Tetanus in the United States Army in World War II, Bull. U. S. Army M. Dept. **7**:371 (April) 1947.

early immunization toxoids of these types had been used for about 75 per cent of the injections reported and were responsible for 90 per cent of the sensitivity reactions observed.

Influenza vaccine has also produced allergic reactions, as reported by Curphey [20] and Salk.[21] That vaccination, insect bites and unknown toxins are suggested in the dermatologic texts as possible etiologic agents or factors in the production of the ordinary childhood type of urticaria pigmentosa bears mentioning at this time.

Summing up our speculation concerning etiology, then, we have a patient who acquired urticaria pigmentosa after a reaction to tetanus toxoid, with apparently an exacerbation or aggravation of the eruption several years later after an influenza vaccine injection, to produce what we have called a case of telangiectasia macularis eruptiva perstans (F. P. Weber). The literature seems to support our theory of the causation in this case. Unfortunately, we did not suspect this origin at the time the patient was available. Accordingly, we again have an incompletely worked-up case of generalized telangiectasia with no skin tests for sensitivity to tetanus toxoid or influenza vaccine and no investigation for reagins in the blood. Also, the histologic sections revealed no endarteritis or other visible damage to the blood vessels due to some toxin or toxin-producing agent, as advocated by Stokes.[12] We can, however, speculate a little farther and surmise that in this case some allergic phenomenon did take place as a result of the reactions to the tetanus toxoid and possibly the influenza vaccine and that the skin was one of the so-called shock tissues which manifested the allergic phenomenon by the clinical picture presented. The persistent sequelae of this allergic phenomenon amount to a pronounced generalized telangiectasia and a hypersensitivity of the skin to heat and trauma. At this point we must fall back on Becker's [13] suggestion of an inherent predisposition or we must assume an individual susceptibility to explain why this phenomenon has not occurred more frequently among the great numbers of people who have now been exposed to tetanus toxoid and influenza vaccine immunizations.

The histopathology of the reported cases of essential or idiopathic generalized telangiectasia can be summed up rather briefly by grouping the cases rather than describing each one individually. Referring to Becker's [13] table 1 again, we find that in by far the majority of the cases reported the histopathologic picture was not reported. In a second group, in which associated syphilis was reported and the histopathologic features were given, there were described in most endarteritis and periarteritis of the vascular supply of the skin, low grade perivascular round cell infiltration, new formation of vessels in the affected skin and some ectasia of the uninvolved vessels, with slight variation in degree of these observations from case to case. A final group showed only dilatation and

20. Curphey, T. J.: Fatal Allergic Reaction Due to Influenza Vaccine, J. A. M. A. **133**:1062 (April 12) 1947.

21. Salk, J. E.: Reactions to Influenza Virus Vaccines, J. A. M. A. **134**:393 (May 24) 1947.

proliferation of the vessels of the cutis with or without lymphocytic perivascular infiltration. In contrast to the above observations, examination of the reaction in our case did not reveal any remarkable dilatation or proliferation of the vessels of the cutis, nor did it reveal any endarteritis or other changes in the vessel walls. It did disclose slight round cell perivascular infiltration, a focal increased melanin pigmentation in the basal cell layer of the epidermis and a moderate number of chromatophores in the cutis. In addition, there was an infiltrate, chiefly in the upper part of the cutis, arranged in columns and strands between the collagen fibers and about the blood vessels which was found to be composed of mast cells by polychrome methylene blue staining (fig. 4).

This observation of numerous mast cells was most welcome because it seemed to classify our case as urticaria pigmentosa or at least as an urticaria-pigmentosa-like condition. A disturbing element was the interjection in the literature of Stokes's [12] description of a pronounced general increase in mast cells throughout the corium and especially conspicuous in the deeper layers and around the large capillaries in his case of syphilis with generalized telangiectasia. Especially disturbing was the observation that McCarthy,[22] in describing the histopathology of poikiloderma atrophicans vasculare, stated that numerous mast cells may be found in this disease. The Atlas of Dermal Pathology [23] stated that mast cells are rather numerous in syphilis and other granulomas but are without diagnostic significance except in urticaria pigmentosa, where they occur in dense, tumor-like masses. According to Macleod and Muende,[24] mast cells are invariably present in the healthy corium and subcutaneous tissue, though not as a rule in large numbers. They are especially numerous in the neighborhood of the blood vessels, hair follicles and sebaceous glands. They are found in quantities in the skin of pigmented regions, such as the dartos of the scrotum and the areolas of the nipples, and on this account it has been suggested that they have some relation to pigmentation of the skin. Mast cells are present also in various pathologic conditions, but only in urticaria pigmentosa are they numerous enough to be of diagnostic value. In the healthy corium it is unusual to find more than one mast cell per microscopic field and when several appear a pathologic condition is indicated. Erythema multiforme and tuberculosis cutis frequently show an increase of mast cells most pronounced in the neighborhood of blood vessels. Also, according to Macleod and Muende, the significance of the observation of mast cells is still not understood and its inconstancy renders it of little

22. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, pp. 79 and 172.

23. Montgomery, H., and others: Atlas of Dermal Pathology, prepared [at the Army Institute of Pathology] by the Registry Committee on Dermal Pathology of the American Academy of Dermatology and Syphilology, Washington, D. C., Registry Press, 1948, p. 54.

24. Macleod, J. M. H., and Muende, I.: Practical Handbook of the Pathology of the Skin, ed. 3, New York, Paul B. Hoeber, Inc., 1946, pp. 132, 134 and 154.

diagnostic value except in urticaria pigmentosa. McCarthy [22] also said that mast cells may be found in normal tissue as well as in many diseases, but he failed to state, as did Macleod and Muende, that only in urticaria pigmentosa are they of diagnostic significance. He described a nevus type of childhood urticaria pigmentosa in which the mast cells form localized tumor-like masses and an adult type in which the collections of mast cells not only vary from time to time but also may even be absent early in the disease only to be found later in characteristic numbers and when found are usually seen to be scattered diffusely through the cutis but chiefly perivascular.

There has been much discussion and difference of opinion with regard to the origin, nature and function of mast cells. Macleod and Muende [24] said that there are two chief opposing views: (1) that these cells are derived from blood and are leukocytes with basic granules and (2) that they are a form of connective tissue cell. Macleod and Muende [24] said that both views seem to be correct but that these cells are not necessarily derived one from the other. The mast cells of Ehrlich are a form of leukocyte, while the mast cells in the corium are not leukocytes but peculiar connective tissue cells with basophilic granules. They expressed the further belief, as hypothesized by Audry, that in both the leukocyte and the connective tissue mast cell the protoplasm has undergone a chemical change, possibly degenerative, whereby basophilic granules have been produced. Macleod and Muende seemed to ascribe a pathologic function to the tissue mast cells. Jorpes,[25] with the aid of Holmgren and Wilander,[26] claimed that the granular substance of the mast cell is the anticoagulant, heparin. He postulated that the mast cells, or "heparinocytes," because of their position around the capillaries and the small blood vessels without a muscular coat, are able to void their granular contents into the perivascular tissue juices, or almost directly into the blood stream; therefore, he suggested that these cells may have a physiologic function to fulfil to the advantage of the blood circulation.

Jorpes [25] seemed to go a little too far in stating that "urticaria pigmentosa is due to the local overproduction of heparin in the skin" and especially in stating that "the appearance of multiple petechial hemorrhages all over the body in this disease is therefore not surprising." If the granules of the tissue mast cells are in fact heparin, it is truly surprising that there are no hemorrhages from the capillaries in urticaria pigmentosa or in telangiectasia macularis eruptiva perstans; however, neither clinically nor histopathologically are these diseases hemorrhagic. It is true that one might speculate on the physiologic function of the "heparinocytes" and state that perhaps they prevent thromboses in the telangiectatic vessels of these diseases.

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25. Jorpes, J. E.: Heparin in the Treatment of Thrombosis: An Account of Its Chemistry, Physiology and Application in Medicine, ed. 2, 1946, New York, Oxford University Press, chap. 3, pp. 57-68.

26. Holmgren, H., and Wilander, O.: Beitrag zur Kenntnis der Chemie und Funktion der Ehrlichschen Mastzellen, Ztschr. f. mikr.-anat. Forsch. **42**:242, 1937; cited by Jorpes,[25] p. 60.

Macleod and Muende [24] told us that urticaria pigmentosa is most probably a nevoid condition and that it has been suggested that the urticarial wheals which develop as a result of rubbing or occasionally from exposure to heat are due to toxic action of liberated mast cell granules.

In the light of recent investigations [27] concerning the physiologic chemistry of the enzyme hyaluronidase and the "mucopolysaccharides" hyaluronic acid and chondroitin sulfuric acid it might be suspected that the mast cells or "heparinocytes" have a very definite physiologic function to fulfil. The biologic function of hyaluronic acid and the similar compounds hyaluron and chondroitin sulfuric acids appears to be mainly architectural, with the provision of a normal gel-like ground substance for connective tissue everywhere in the body. The enzyme hyaluronidase hydrolyzes these "mucopolysaccharides" and increases the permeability of the connective tissues and perhaps of the capillaries. All three of these substances have been found in skin as well as in other tissues and organs. Heparin, among other things, inhibits the action of hyaluronidase; so perhaps the mast cells or "heparinocytes," which are so numerous in urticaria pigmentosa, are performing a physiologic function by inhibiting the action of an excess of hyaluronidase, which may be found to be playing at least a part in the pathologic physiology of this disease. This theory, of course, can be proved or disproved only by a careful chemical analysis of the skin in a case of urticaria pigmentosa and comparison of the observations with those made in normal skin.

Thus, telangiectasia macularis eruptiva perstans seems to be a distinct clinical entity among the generalized telangiectatic diseases. Its etiology is still obscure. It does not seem to fit too well into any of the four etiologic types—infectious, endocrinous, cardiovascular or neurogenous generalized telangiectasia—as suggested by Becker.[13] Perhaps a fifth type of allergic or toxic generalized telangiectasia must be added, with the remembrance that Lanceplaine [11] in 1904 included the term "toxic" in his classification and that Stokes [12] in 1915 discussed the relation of toxins or toxin-producing agents to the development of generalized telangiectasia.

SUMMARY

The rarity of the disease and the sparsity of the literature on the subject of telangiectasia suggested the possible need for a review of the literature on this condition, the presentation of another case and a discussion of its relation to other forms of generalized telangiectasia.

In 1930 Weber [3] first used the term "telangiectasia macularis eruptiva perstans" to describe a very rare telangiectatic, relatively pigmentless variety of urticaria pigmentosa of adults. A search of the literature by Weber revealed that, though it is a relatively rare condition, it had for a long time been recognized in France under some name such as "essential telangiectasias in acquired plaques."

27. Hyaluronidase, a Monograph from the Clinical Research Division, Schering Corporation, Bloomfield, New Jersey, 1947.

A typical case of telangiectasia macularis eruptiva perstans is reported. No specific etiologic factor was found, though the history suggests some relation to an influenza vaccine injection or to a subsequent attack of influenza. However, the case had been diagnosed as urticaria pigmentosa four and one-half years prior to the alleged offending influenza vaccine injection. The patient stated that the earlier eruption, which appeared after a tetanus toxoid reaction, was an entirely different kind of rash from the later one. A polychrome methylene blue–stained biopsy section revealed numerous mast cells, which seemed to support the diagnosis of urticaria pigmentosa, or, as designated by Parkes Weber, "telangiectasia macularis eruptiva perstans," an adult type of urticaria pigmentosa. No specific therapy was found, and no improvement in the case occurred, though some slight symptomatic relief from pruritus was obtained from the use of diphenhydramine (benadryl®).

A differential diagnosis of telangiectasia macularis eruptiva perstans is given. The etiology and pathology of generalized telangiectasia are reviewed, and an attempt is made to discuss the possible causation and pathogenesis of the case presented. The history of the patient and the literature seem to support the theory that this condition may be a manifestation of an allergic or toxic reaction, although further investigation is needed.

A discussion of the theories of the origin and significance of mast cells is given.

Clinical Notes

LOCAL CUTANEOUS SENSITIVITY TO METHAPYRILENE

Report of a Case

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AND
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Since the introduction of the antihistamine drugs into our therapeutic armamentarium for the treatment of suspected or actual allergic conditions, there have been relatively few reports of dermatologic complications following their local use.

In the few reports available, most complications have been observed to follow ingestion of the drug.[1] Epstein,[2] however, reported a case of dermatitis due to ingestion of prophenpyridamine (trimeton®), in which subsequently a positive reaction to patch testing to the tablet was obtained. Strauss[3] reported a case of eczematous contact type allergy to tripelennamine (pyribenzamine®) ointment, likewise verified by a positive patch test reaction.

A review of the literature revealed no case of proved dermatitis caused by the local application of methapyrilene (histadyl®) cream, although Lewis[4] observed one incident of sensitivity to methapyrilene when the drug was applied in a patch test.

The following report is of a case in which an eczematoid dermatitis resulted from the local use of methapyrilene cream.

REPORT OF A CASE

Present Illness.—G. T., a 64 year old white man, was referred to us on Feb. 4, 1949, by Dr. Oscar Bloch Jr. One week prior the patient had awakened one morning scratching what he called "hundreds of little pimples" on his forehead. He applied cold compresses of aluminum acetate solution to these for relief of the itching. Later he called his physician, who, on Feb. 3, 1949, prescribed methapyrilene cream, which was applied several times that day.

Past History.—While this patient gave no personal history of atopies, his mother probably had had an allergic eczema, and in July 1948 he had had a "breaking out and burning" in his groin which he had treated himself with calamine lotion, compresses of boric acid solution and norcohol® (a proprietary rubbing alcohol containing 70 per cent alcohol). The eruption had gradually spread to his face and eyes, whereupon he called a dermatologist, who prescribed several different local preparations, including an ointment subsequently found by us to contain equal parts of boric acid ointment and methapyrilene cream.

1. Epstein, E.: Dermatitis Occurring During Therapy with Tripelennamine Hydrochloride ("Pyribenzamine Hydrochloride"), J. A. M. A. **134**:782 (June 28) 1947. Harris, M. C., and Shure, N.: Eczematoid Dermatitis Following Ingestion of "Pyribenzamine Hydrochloride," N.N.R. Tablets, J. Allergy **18**:408 (Nov.) 1947. Rattner, H., and Graffin, J.: Dermatitis Due to Pyribenzamine, Am. Pract. **2**:754 (July) 1948. Levin, L.; Kelley, J. F., and Schwartz, E.: A Clinical Evaluation of Neo-Antergan and Antistine in the Treatment of Ragweed Hay Fever, New York State J. Med. **48**:1474 (July 1) 1948.

2. Epstein, E.: Dermatitis Due to Anti-Histaminic Agents, J. Invest. Dermat. **12**:151 (March) 1949.

3. Strauss, M. J.: Eczematous Contact-Type Allergy to Pyribenzamine, J. Invest. Dermat. **11**:155 (Sept.) 1948.

4. Lewis, G. M.: Personal communication to the authors.

The eruption then had spread rapidly over almost his entire body. This had finally cleared up completely after several months of treatment, including roentgen ray therapy. There had been no recurrences until the onset of the present illness. This may have been initiated by the wearing of an old hat that had previously been contaminated with this boric acid–methapyrilene cream combination.

Examination.—When first seen by us the patient presented a weeping, vesicular, erythematous eruption, confined for the most part to the face, eyes, neck, ears and forehead. The eyes were closed from the pronounced edema which involved the entire face. There was a blotchy, erythematous, macular eruption over the shoulders. A diagnosis of dermatitis venenata was made.

Under bland local therapy alone the patient's condition decidedly improved in several days, and in a few weeks he was completely free of his dermatitis.

Investigative Data.—Routine Patch Tests: While performing a group of diagnostic patch tests on this patient, we found that he gave positive reactions to the following: methapyrilene (histadyl®) cream (Lilly), ointment containing equal parts of boric acid ointment and methapyrilene cream, and norcohol.®

Specific Patch Tests: To determine the specific ingredient in the methapyrilene cream to which the patient was allergic, patch tests to both 2 per cent methapyrilene solution and the cream base [5] were performed. The patch test to the solution produced a positive reaction, as evidenced by a papular erythema, studded with tiny vesicles, at the end of forty-eight hours. The patch test reaction to the cream base was negative.

Results of Patch Tests to Other Antihistamine Preparations: In order to determine whether or not local cutaneous sensitivity to one antihistamine drug precluded sensitivity to others, the patient was given patch tests to phenindamine (thephorin®), diphenhydramine (benadryl®) and tripelennamine ointments. All reactions were negative at the end of forty-eight, seventy-two and ninety-six hours.

Attempts to Produce a Generalized Eruption or Flare of Local Patch Test Reactions by Ingestion of Methapyrilene: Attempts to produce a generalized reaction or flare of a local patch test reaction by local ingestion of methapyrilene failed.

Attempts to Produce An Eruption by Ingestion of Other Antihistamine Drugs: In order to ascertain whether or not the patient had a sensitivity to other antihistamine preparations when ingested, he was given, at twenty-four to thirty-six hour intervals, the following antihistamine drugs: phenindamine, diphenhydramine, tripelennamine, pyranisamine (neoantergan®), methaphenilene (diatrin®), prophenpyridamine and thonzylamine (neohetramine®). No allergic reactions were noted.

SUMMARY

A case of local cutaneous sensitivity to methapyrilene is reported.

Patch test to the 2 per cent methapyrilene solution elicited positive reactions, whereas that to the cream base produced negative ones.

Patch tests to other antihistamine creams and ointments were negative.

Methapyrilene and seven other antihistamine preparations given by mouth produced no observable cutaneous reactions in this patient.

CONCLUSIONS

A case of local cutaneous sensitivity to methapyrilene is reported. To our knowledge, this is the first available report in the literature.

Ingestion of this antihistamine drug produced no observable cutaneous response.

Local cutaneous sensitivity to one antihistamine preparation does not imply sensitivity to others.

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5. The methapyrilene solution and cream base no. 5 were supplied by Eli Lilly & Company, Indianapolis.

APPLICATION OF POTASSIUM HYDROXIDE TO THE SKIN AS AN AID IN THE DIRECT EXAMINATION OF SCALES FOR FUNGI

ALBERT M. KLIGMAN, Ph.D., M.D.*
PHILADELPHIA

The potassium hydroxide mount is the standard preparation for the direct microscopic examination of fungi in skin and nail scrapings. Often the discovery of hyphal elements in a ringworm lesion depends on the enthusiasm and vigorousness of the person doing the scraping. This point holds particularly true in chronic hyperkeratotic palmar or plantar dermatophytosis in which hyphae may be scanty. The collection of copious scrapings from such cornified lesions is not readily achieved by the usual method of scraping the unprepared skin with a blunt knife.

Scraping is greatly facilitated and large quantities of the material may be quickly collected with use of the following simple modification. A few drops of 10 per cent potassium hydroxide such as is ordinarily used to mount scrapings are placed directly on the skin over the peripheral portion of the lesion. Thus prepared, the lesion is scraped in the usual fashion. Because of the macerating and keratolytic effect of the hydroxide, a large quantity of corneous material comes away on the knife. Practically all of it sticks to the knife and is easily transferred to the drop of potassium hydroxide on the slide.

After the scraping, the excess of potassium hydroxide solution should be removed with a sponge saturated with water or alcohol. Patients do not mind the direct application of hydroxide to the skin, and no untoward effects have been observed from intelligent use of this method. Potassium hydroxide obviously should not be placed on acutely inflamed skin, nor is its use required in securing material for examination of scales from such lesions. The method described is particularly for hyperkeratotic chronic eruptions. Material collected in this way should not be used for culturing. A separate sample is required for this last-mentioned procedure. Although, in addition to scrapings cultures should routinely be made on suspected lesions, the direct examination of scrapings has yielded a much higher percentage of positive observations in the experience of most workers.

*Senior Research Fellow, United States Public Health Service.

This study was one of various studies supported by the Research and Development Board, Department of the Army.

From the Department of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Donald M. Pillsbury, M.D., director.

UNIVERSAL ICHTHYOSIS

Occurrence in Three Siblings Without Family History of Major Dermatoses

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Cockayne suggested that all unusual cases of hereditary dermatoses be reported; therefore the following cases are reported.

As may be seen from the family chart, there was no previous history of any generalized or severe congenital dermatosis in the family history.

D. B., a white boy aged 5 years, when first seen, in April 1944, had a universally moderately erythematous, dry ichthyotic skin with pronounced scaling. Although the hair on his scalp was slightly sparse, the other dermal appendages were essentially normal. The nails were well formed. A younger brother aged 1½

Fig. 1.—D. B., aged 5, shows the severe confluent ichthyosis which was generalized and similar in type in all 3 of the siblings.

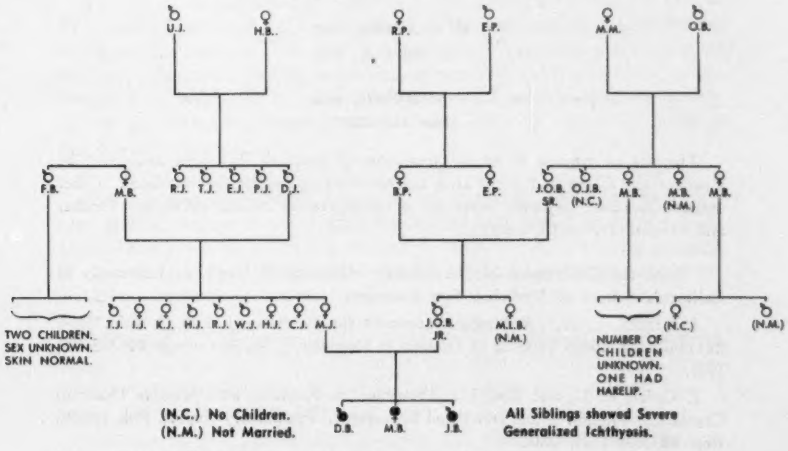

Fig. 2.—Family chart for the 3 patients whose cases are reported.

years and a sister aged 3 years showed essentially the same cutaneous picture. The patient was put on treatment with high doses of vitamin A without any improvement. Unfortunately no biopsy specimen was obtained.

"Authorities are agreed that ichthyosis vulgaris is inherited and that it often skips one or more generations, but the published pedigrees are disappointingly few, perhaps because it is one of the commonest of the inherited defects of the skin. Single cases are not uncommon, and, though less often met with, there are many records of two or more in a sibship, but the absence of a family history of ichthyosis may be due to its having been transmitted for two or three generations by apparently normal individuals. Gaskoin has collected many records, but his confusion of this defect with congenital ichthyosiform erythrodermia makes it difficult to classify those occurring only in a single sibship, and many of the pedigrees of those occurring in more than one generation are incomplete." [1]

"It is probable that the defect, whether inherited by direct or interrupted descent, is due to the same gene or genes, but if so an explanation must be sought for its regular dominance in some families and its irregular dominance in others. There may be an inhibiting gene inherited independently in those with interrupted descent, or ichthyosis may require the presence of two independent genes for its development, one very common and one uncommon amongst the general population. On the other hand, ichthyosis inherited by direct descent may be genetically different from that inherited by indirect descent." [2]

Three severe, unusual cases of ichthyosis are reported in siblings with no previous family history of a major dermatosis in the past four generations.

1. Ichthyosis Vulgaris, in Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, New York, Oxford University Press, 1933, p. 211.

2. Sex-Linked Recessive Form, in Cockayne,[1] p. 213.

VITAMIN D_2 IN THE TREATMENT OF PSORIASIS

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F. G. NOVY, Jr., M.D.
and
J. H. BENNETT, M.D.
SAN FRANCISCO

The use of vitamin D in the treatment of psoriasis has been advocated by Krafka [1] and Ceder and Zon [2] after the encouraging results they obtained. Other authors, however, reported equivocal or unimpressive results (Wright,[3] Pascher and co-workers [4] and Clarke [5]).

From the Department of Dermatology, Division of Medicine, University of California School of Medicine, San Francisco.

1. Krafka, J., Jr.: A Simple Treatment for Psoriasis, J. Lab. & Clin. Med. **21**:1147-1148, 1936; Vitamin D Therapy in Psoriasis, J. M. A. Georgia **30**:398-400, 1941.

2. Ceder, E. T., and Zon, L.: Treatment of Psoriasis with Massive Doses of Crystalline Vitamin D and Irradiated Ergosterol: Preliminary Report, Pub. Health Rep. **52**:1580-1584, 1937.

3. Wright, C. S.: Vitamin D Therapy in Dermatology, Arch. Dermat. & Syph. **43**:145-154 (Jan.) 1941.

One of the drawbacks of using vitamin D has been the possibility of toxic reactions. Recently, refinements of production have eliminated some of the toxic substances responsible for undesirable side effects.

In an attempt to evaluate the effects of a modern preparation of vitamin D_2, a limited number of unselected patients with psoriasis were treated with a sterile solution of persic oil and ether containing 600,000 U. S. P. units of crystalline vitamin D_2 per cubic centimeter.[6]

METHOD

Prior to treatment, the history of each patient was taken. A complete physical examination was performed, after which a skin specimen was taken for biopsy. A photograph of each patient was made. Laboratory examinations included blood serologic tests for syphilis, determination of serum calcium, potassium, proteins and hemoglobin value, white blood cell count and urinalysis. Laboratory examinations were repeated every three to four weeks and again on completion of treatment.

SUBJECTS

Because of budgetary limitations only a small number of patients could be studied. Seven patients, ranging in age from 27 to 63 years, were treated. Five of the patients were white, and two were Negroes; four were male, and three, female. All had had psoriasis from eight months to ten years, and all but one had had several forms of therapy prior to this trial. One patient gave a history of familial psoriasis (father, brother, aunt); one patient had arthritis accompanying psoriasis.

TREATMENT

Intramuscular injections, twice a week, of 600,000 units of vitamin D_2 were given. No other form of therapy was used, with the exception of the application of bland, nonmedicated ointments. The seven patients received 6, 10, 13, 16, 18, 20 and 23 total injections, respectively.

RESULTS

One patient stopped treatment after only three weeks for nonmedical reasons. There was no change in his lesions. None of the remaining six patients showed any significant changes. One, who had received 13 injections, noticed a slight relief of pruritus and a decrease in scaling; another, who had received 16 injections, showed some clearing in the center of the large plaques. None of the patients showed any evidence of toxicity, as manifested either by clinical symptoms or by laboratory examinations.

CONCLUSIONS

This report is not submitted because of any statistical significance, as there is none in data concerning such a small, uneven and uncontrolled group of patients. It is merely presented as another instance of unsuccessful therapy for psoriasis. It also might add some information on the lack of toxicity of the preparation used under the circumstances described.

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4. Pascher, F.; Silverberg, M. G.; Marks, I. E., and Markel, J.: Therapeutic Assays of the New York Skin and Cancer Unit, Post Graduate Medical School, New York University–Bellevue Medical Center: Assay II—Calciferol (D_2), J. Invest. Dermat. **12**:193-202, 1949.

5. Clarke, G. E.: Treatment of Psoriasis with Concentrated Viosterol, Arch. Dermat. & Syph. **41**:664-666, 1940.

6. Metadee,® furnished by Sharp & Dohme, Inc., Philadelphia.

RESIN OF PODOPHYLLUM IN TREATMENT OF MOLLUSCUM CONTAGIOSUM

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GREENSBORO, N. C.

The treatment of molluscum contagiosum by local destructive measures is frequently a very disturbing office procedure because of the multiplicity of lesions and because many of the patients are so young that cooperation, with the use of a treatment which is painful, cannot be expected.

This report deals with the treatment of a patient with multiple lesions of molluscum contagiosum by local applications of resin of podophyllum solution. The

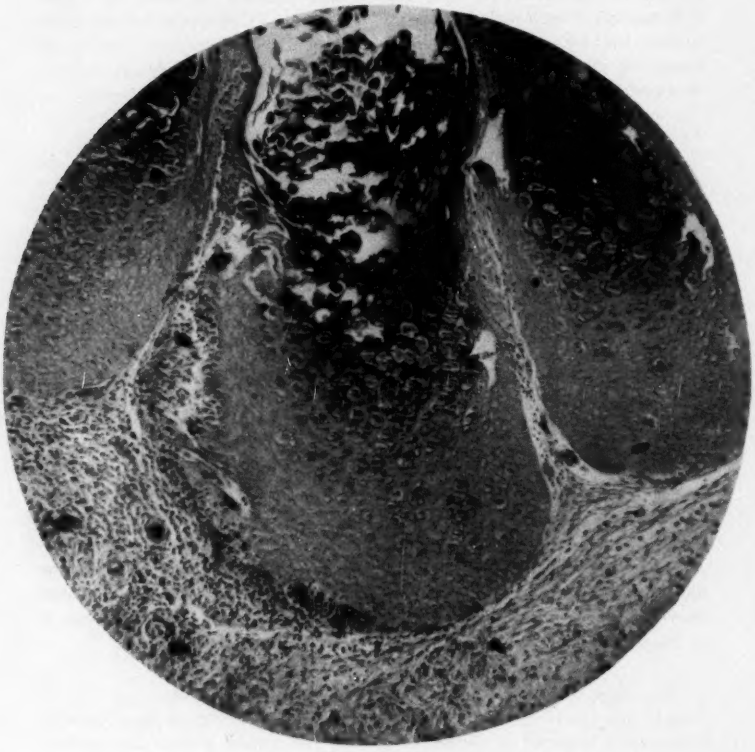

Fig. 1.—Microscopic appearance of representative lesion.

results were so striking that it is felt that such a treatment regimen may offer a satisfactory solution for dealing with multiple lesions of molluscum contagiosum in young children.

REPORT OF A CASE

A highly nervous 12 year old boy was first seen by me on Jan. 17, 1949. There were between forty and fifty typical lesions of molluscum contagiosum over the left trunk, two lesions on the right side of the back at the level of the fourth rib and two other lesions on the medial aspect of the left knee. On the left portion

of the trunk there was a large lesion about 1 cm. in diameter at the level of the costal margin in the midaxillary line, and there were numerous satellite lesions scattered over the left part of the chest and abdomen. The lesions had been appearing for a period of about one month.

One lesion was excised, and the histopathologic picture, which is typical of molluscum contagiosum, is demonstrated in figure 1.

Because of the patient's extreme degree of apprehension and nervousness, it was obvious that it would be impossible to treat these lesions by local destructive methods without giving the patient a general anesthetic.

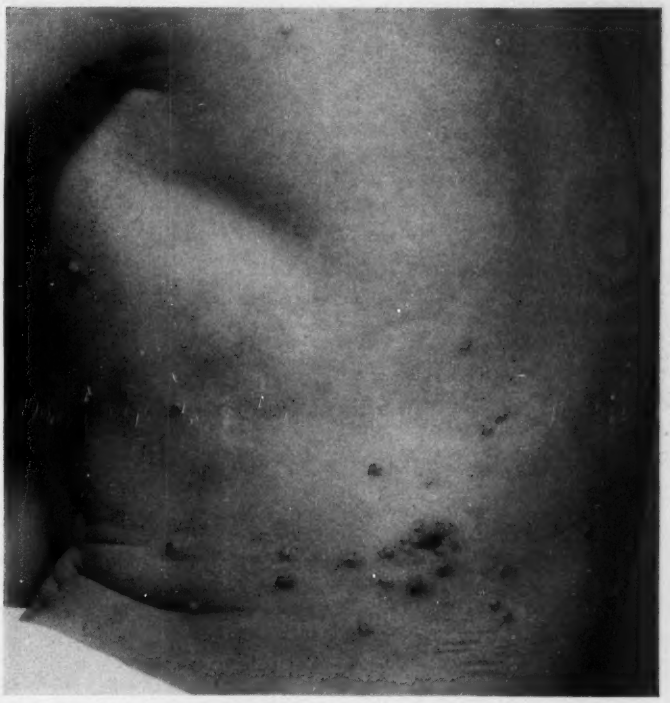

Fig. 2.—Clinical appearance before resin of podophyllum therapy.

I recalled the work of Sullivan and King [1] in treating condylomata acuminata and verrucae vulgares with local applications of resin of podophyllum. They had found that the resin of podophyllum in 95 per cent alcohol was more effective than was resin of podophyllum in an ointment base. I therefore decided to use a solution containing 20 per cent of the resin of podophyllum in 95 per cent alcohol.

From the time of the original visit until February 17, 20 per cent resin of podophyllum in 95 per cent alcohol was applied to the lesions twice weekly. After

1. Sullivan, M., and King, L. S.: Effects of Resin of Podophyllum on Normal Skin, Condylomata Acuminata and Verrucae Vulgares, Arch. Dermat. & Syph. **56**:30 (July) 1947.

two or three applications, most of the lesions became quite dry and in some instances could easily be "wiped off." Other lesions became soft and macerated and gradually diminished in size. From February 17 until March 21 resin of podophyllum was applied weekly. At the end of this period, several lesions which had appeared to have been almost destroyed seemed to be enlarging and a few new lesions had appeared. At that time the frequency of applications was increased to twice a week, and this schedule was continued until April 25, 1949. On that date the lesions appeared to be completely destroyed. Slight atrophy was visible at the sites of most of the previous lesions. The patient has subsequently been under observation for

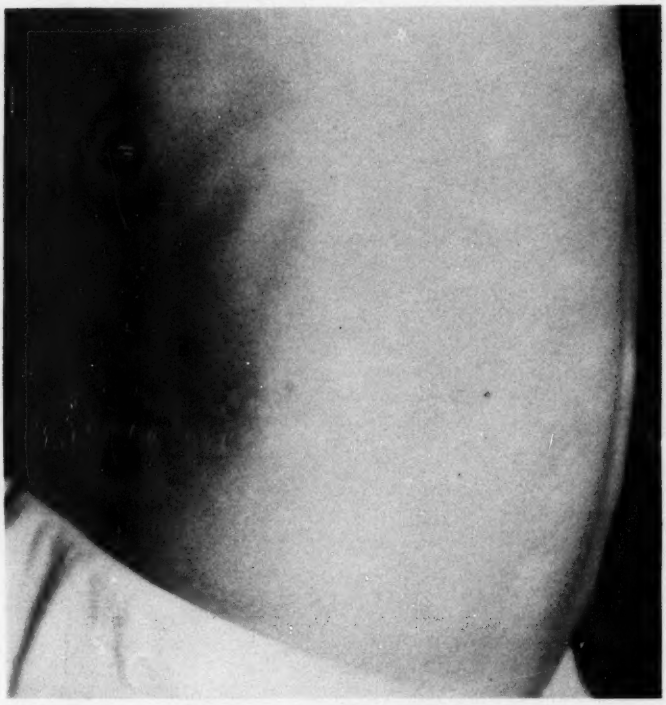

Fig. 3.—Clinical appearance after resin of podophyllum therapy.

one month, and there has been no recurrence of any lesion nor have any new lesions developed to the time of writing.

Figure 2 is a photograph of the left portion of the trunk at the time treatment was commenced, and figure 3 is a photograph of the same area taken on April 29, four days after the last application of resin of podophyllum.

COMMENTS

It is unfortunate that I have seen no other patients with molluscum contagiosum in the treatment of whom resin of podophyllum might have been used. This report, however, may stimulate use of this form of treatment in various hands and lessen the period necessary for the evaluation of the effectiveness of this form of therapy.

It seemed readily apparent in our patient with molluscum contagiosum that if the resin of podophyllum were not applied with sufficient frequency regrowth would occur in lesions which had been partially destroyed. It was noted that the smaller lesions disappeared first, and it seems a logical assumption that only the superficial cells were destroyed as a result of each application.

It is probably a perfectly safe procedure to allow the applications of resin of podophyllum to be made at home in instances in which treatment can be made intelligently and reliably. If one may judge from the observations made in this case, it would seem advisable to make the applications at least twice weekly until the lesions have completely disappeared.

CONCLUSIONS

A patient with multiple lesions of molluscum contagiosum was successfully treated with topical application of 20 per cent resin of podophyllum in 95 per cent alcohol from once to twice a week over a period of a little more than three months.

Visible effects on the superficial parts of the lesions were definite within a week after the first application of the resin of podophyllum.

It would seem advisable to apply the resin of podophyllum at least twice a week, since some of the lesions showed progression when the frequency of topical application was reduced to once a week.

This method probably is a safe home therapeutic procedure in instances in which there is sufficient intelligence and reliability. No discomfort of any significance was experienced by our patient.

It is hoped that this report will stimulate trial of this form of therapy in different hands and will lead to a rapid evaluation of its effectiveness as well as stimulate interest in the general field of investigation of the usefulness of local application of cytotoxic drugs on metaplastic and dyskeratotic cells.

ADDENDUM.—Since the submission of this report for publication, 2 other patients have been treated for molluscum contagiosum with 20 per cent resin of infant podophyllum in 95 per cent alcohol. One was an 18 month old girl who had had lesions of molluscum contagiosum for five to six weeks. The other was a 2 year old boy who had had lesions for two weeks. In both instances the lesions were scattered over the upper right part of the chest with some present in the right axilla.

In both instances applications were made at home every other day. In the first patient the lesions had completely disappeared within one month, and in the second patient, in three weeks. In both instances a rather severe dermal reaction developed in the right axilla as a result of the application of resin of podophyllum, and this dermatitis had to be treated after the lesions of molluscum contagiosum had disappeared. No dermal reaction of any significance developed from the application of resin of podophyllum except in the moist intertriginous areas of the axillas.

363 North Elm Street.

A CONTROLLED CLINICAL EVALUATION OF THEPHORIN® OINTMENT IN THE RELIEF OF PRURITUS

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PHILADELPHIA

Clinical investigations by Shelmire,[1] Wooldridge and Joseph[2] and Laymon and Schmid[3] indicate that phenindamine (thephorin®) ointment is a valuable agent in the relief of pruritus. In order to arrive at a true evaluation of the effectiveness of this preparation, a controlled clinical study was undertaken.

MATERIALS AND METHOD

Phenindamine (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene) is a clear, colorless, water-soluble, crystalline antihistaminic compound.[4]

Forty-one patients were studied. In 20 cases bilateral involvement made it possible to apply the ointment containing 5 per cent phenindamine to lesions on one side of the body and the ointment base alone to comparable lesions on the opposite side for control, as suggested by Sulzberger.[5] For the 16 patients presenting only a single lesion or when comparable areas did not exist, the phenindamine and control ointments were alternated at weekly intervals without the knowledge of the patient.

Results in a Controlled Clinical Evaluation of Phenindamine Ointment in the Relief of Pruritus

Diagnosis	No. of Patients Treated	Average Duration of Condition	Average Duration of Treatment	Average Percentage Pruritus Relieved by 5 Per Cent Phenindamine Ointment	Average Percentage of Pruritus Relieved by Control Base Alone
Circumscribed neurodermatitis (lichen simplex chronicus)	12	3 yr.	29 days	58	59
Atopic dermatitis (disseminated neurodermatitis)	10	12 yr.	40 days	46	46
Miscellaneous pruritic dermatoses	14	3 yr. (2 wk. to 17 yr.)	28 days	37	41
Pruritus ani	5	4 yr.	24 days	60	..
All cases (excluding pruritus ani cases)	36	6 yr.	32 days	47	49

* Statistical analysis of the data by means of "Student's" test elicited a "t" value of 0.8223, $P = 0.4$ (difference between the phenindamine series and the control series not statistically significant).

The materials used in this study were supplied by Hoffmann-LaRoche, Inc., Nutley 10, N. J.

From the Department of Dermatology and Syphilology, School of Medicine, Donald M. Pillsbury, M.D., director, University of Pennsylvania.

1. Shelmire, B.: Topical Treatment with Thephorin, Postgrad. Med. **4**:443-446 (Nov.) 1948.

2. Wooldridge, W. E., and Joseph, H. L.: Disseminated and Circumscribed Neurodermatitis Treated with Phenindamine (Thephorin®), Arch. Dermat. & Syph. **60**:390-403 (Sept.) 1949.

3. Laymon, C. W., and Schmid, J. F.: The Topical Application of Thephorin in Pruritic Dermatoses, Ann. Allergy **6**:638-644 (Nov.-Dec.) 1948.

4. Lehmann, G.: Pharmacological Properties of a New Antihistaminic, 2-Methyl-9-Phenyl-2,3,4,9-Tetrahydro-1-Pyridindene (Thephorin) and Derivatives, J. Pharmacol. & Exper. Therap. **92**:249-259 (March) 1948.

5. Sulzberger, M. B.; Baer, R. L.; Kanof, A., and Lowenberg, C.: Methods for the Rapid Evaluation of the Beneficial and Harmful Effects of Agents Applied to the Human Skin, J. Invest. Dermat. **7**:227-238 (Oct.) 1946.

The subjects were told that the tubes contained "slightly different forms of the same medication." Care was taken to see that no hint regarding the nature of the contents was disclosed. The tubes containing the control and medication were identical in appearance and were unlabeled. There was no noticeable difference in texture, odor or color between the phenindamine and control ointments. Each patient was interviewed and examined weekly throughout the period of study by the same investigator. During this experiment no other form of therapy, external or internal, was allowed. The only instructions given were that the ointment should be applied as needed for relief of itching. The patients were asked to evaluate the antipruritic effectiveness of the two preparations on a percentage basis. Absence of relief was considered 0 per cent, and complete relief, 100 per cent.

COMMENT

It is apparent that under the conditions of this experiment both the carbowax® 1500 and vanishing cream bases are fairly efficient agents in the relief of pruritus and that the inclusion of 5 per cent phenindamine adds nothing to this effect. The ability of these bases to relieve itching may be due to the lubricatory action on the skin and the psychogenic effect of their application.

Special notice should be taken of the fact that, although the itching of pruritus ani was much allayed (averaged 60 per cent relief) during the initial days of application of phenindamine, this effect was only transitory. The antipruritic effect was sustained at a high level in only one out of five cases. The results from the pruritus ani series were not included in the final total because of the inconstant action of the medication in this condition.

The possibility that systemic absorption of phenindamine from the treatment site might have had an antipruritic effect on the control area was considered. However, approximately half the patients were treated by weekly alternation of the medication and the control. Thus, any absorbed phenindamine would have had time to be eliminated and would not be expected to affect the control site during the following week.

The development of sensitivity to phenindamine ointment in a substantial number of patients made further study of this preparation inadvisable.

CONCLUSIONS

Phenindamine, 5 per cent, in carbowax® 1500 or in a vanishing cream type base is neither more nor less effective in the relief of pruritus than the unmedicated base alone.

LUPUS ERYTHEMATOSUS FOLLOWING LACERATION BY BROKEN GLASS

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NEW YORK

External irritation as a factor in the causation of lupus erythematosus was presented in a survey by David King-Smith[1] some years ago. He discussed 18 cases in which the onset of the skin eruption was attributable to external irritation. In this series, seven cases followed direct burns (sun, hot fat, steam, water, radiant heat), seven were secondary to mustard gas dermatitis, one to a contact dermatitis from hair dye and two from direct laceration. During the intervening years, 1926 to the present, little direct evidence of the traumatic inception of lupus erythematosus has been advanced. The problem has importance not only from the standpoint of the disease condition but also from the medicolegal aspect. The latter aspect led to a thorough study of a case of lupus erythematosus the origin of which was unequivocally laceration due to broken glass.[2]

From the Department of Dermatology, New York Medical College, Flower and Fifth Avenue Hospitals, Dr. Eugene F. Traub, director.

1. King-Smith, D.: External Irritation as a Factor in the Causation of Lupus Erythematosus Discoides, Arch. Dermat. & Syph. **14**:547 (May) 1926.

2. Coakley, W. A.; Shapiro, R. N., and Robertson, G. W.: Granuloma of the Skin at Site of Injury by a Fluorescent Bulb, J. A. M. A. **139**:1147 (April 23) 1949.

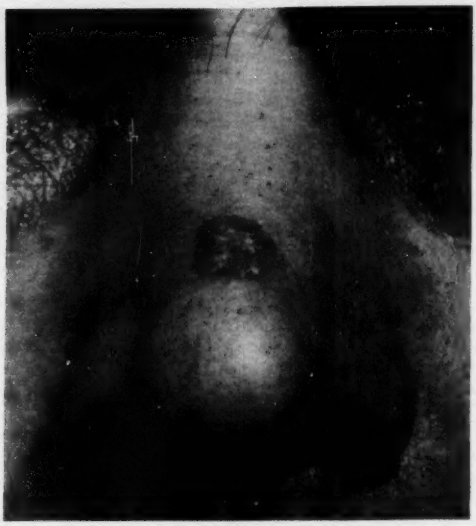

Fig. 1.—Lupus erythematosus on the bridge of the nose at the site of laceration.

Fig. 2.—Biopsy specimen taken from the lesion on the nose, magnified 127 times, showing basophilic degeneration and cellular infiltration in the upper part of the cutis. The epidermis was acanthotic and hyperkeratotic with a small follicular plug. In some areas the basal cell margin was washed out.

REPORT OF A CASE

F. F., a 44 year old white man, received a cut on his nose when a bottle broke and sprayed glass in his face while he was emptying an ashcan into the hopper of a sanitation truck. The injury occurred on Dec. 27, 1949. The skin laceration became inflamed within a day, and within a week a red, slightly swollen area developed at the site of the laceration. Cutaneous examination on Jan. 27, 1950, revealed a longitudinal erythematous infiltration on the bridge of the nose. It measured 15 by 10 mm. Desquamation, plugging of the follicles and atrophy were present (fig. 1). There were no other patches of eruption on the body.

Complete physical examination revealed no previous skin eruption. Biopsy of the lesion was accomplished on February 16. The observations on microscopic examination were reported as follows (fig. 2): The vessels throughout the cutis were dilated. There was a moderate infiltration of small round and wandering connective tissue cells in the upper part of the cutis and about the adnexa. Moderate basophilic degeneration was present in the subepidermal region. The epidermis was acanthotic, the horny layer more densely laminated and the surface verrucous. Beneath the epidermis was clumping of the elastic tissue. A microscopic diagnosis of lupus erythematosus was made.

100 Central Park South (19).

ANGIONEUROTIC EDEMA FOLLOWING PYRIBENZAMINE® THERAPY

Report of a Case

ALVO GUIDUCCI, M.D.
AND
EUGENE F. TRAUB, M.D.
NEW YORK

The widespread use of the so-called antihistamine drugs, including tripelennamine (pyribenzamine®), has brought numerous and varied side reactions to the attention of physicians. Among these side reactions are drowsiness, headache, nausea, dizziness, nervousness, insomnia and dryness of the mouth.[1] Reports of the allergic skin reactions to tripelennamine have been mainly of eczematoid contact type eruptions.[2] Other skin manifestations from the use of tripelennamine have been a pityriasis-rosea-like eruption, reported by Epstein,[3] and a case of a morbilliform eruption which a week later showed the clinical and histological picture of multiple simple angiomas with no telangiectasia, reported by Oppenheim and Yacullo.[4]

From the Department of Dermatology, New York Medical College, Metropolitan Hospital Division.

1. Kennedy, C. B., and Herrington, V. M.: Drug Reactions and Their Treatment with Special Reference to the Use of BAL in Heavy Metal Poisoning, New Orleans M. & S. J. **100**:209-217 (Nov.) 1947. Brown, S. F.: Side Reactions to Pyribenzamine Medication, Proc. Soc. Exper. Biol. & Med. **67**:373-374 (March) 1948. McGavack, T. H.; Weissberg, J., and Boyd, L. S.: Comparison of Toxic Manifestations Produced by Beta-Dimethylaminoethyl Benzhydril Ether Hydrochloride (Benadryl) and Tripelennamine (Pyribenzamine), J. Lab. & Clin. Med. **33**:595-601 (May) 1948.

2. Strauss, M. J.: Eczematous Contact-Type Allergy to Pyribenzamine, J. Invest. Dermat. **11**:155 (Sept.) 1948. Harris, M. C., and Shure, N.: Eczematoid Dermatitis Following Ingestion of "Pyribenzamine Hydrochloride," N. N. R. Tablets, J. Allergy **18**:408-412 (Nov.) 1947.

3. Epstein, E.: Dermatitis Occurring During Therapy with Tripelennamine Hydrochloride ("Pyribenzamine Hydrochloride"), J. A. M. A. **134**:782 (June 28) 1947.

4. Oppenheim, M., and Yacullo, W. A.: Generalized Angiomatosis Simplex Cutis Following an Erythema Morbilliforme Probably Caused by the Use of Pyribenzamine, Brit. J. Dermat. **60**:368-371 (Nov.) 1948.

London and Moody [5] made the initial report of an acute urticarial response following the oral administration of tripelennamine. The rarity of this reaction justifies our reporting a confirmatory case.

REPORT OF CASE

The patient, J. B., a 68 year old Puerto Rican, was admitted to the skin service of the Metropolitan Hospital on Aug. 9, 1949, with a mild but generalized exfoliative dermatitis of three months' duration. Efforts to determine the cause were unsuccessful. Treatment previous to hospital admission had included the use of various antihistamine drugs. On the patient's admission to the hospital aluminum acetate (Burow's) solution in emulsion base was applied locally, and he was given phenindamine (thephorin®) hydrochloride, 25 mg. three times daily. On Oct. 25, 1949, the use of phenindamine was discontinued because of persistent mild nausea, and the administration of tripelennamine hydrochloride, 50 mg. three times a day, was substituted. On Nov. 5, 1949, the patient complained of swelling of the face, a sore throat and difficulty in swallowing. The facial swelling reached huge proportions. Administration of tripelennamine was stopped, and 0.25 cc. of epinephrine hydrochloride 1:1,000 for two doses was administered. The edema began to subside and entirely disappeared in 24 hours. Six days later the patient was given a test dose of 25 mg. of tripelennamine hydrochloride orally. Within three hours, he complained of a "tightness" in his throat, which was considerably milder than the previous attack. Edema of the upper eyelids was noticed and gradually increased so that the following morning the patient was barely able to see. Epinephrine was again administered, and its use resulted in striking improvement. Three days later, a solution of 1 mg. of tripelennamine hydrochloride in 0.1 cc. of distilled water was injected intradermally into the flexor aspect of the forearm. No reaction occurred at the site of injection, but again the lips and upper eyelid became edematous. A Prausnitz-Küstner passive transfer test performed with the patient's serum gave a negative reaction.

SUMMARY

A case of angioneurotic edema due to a so-called antihistamine drug is reported. Tripelennamine was apparently the cause of the intense allergic response.

5. London, I. D., and Moody, M., Jr.: Acute Urticaria Following Pyribenzamine Therapy, J. Invest. Dermat. **13**:217-219 (Oct.) 1949.

DERMATITIS FROM NAIL LACQUER APPLIED TO COSTUME JEWELRY

HOWARD J. PARKHURST, M.D.
TOLEDO, OHIO

Dermatitis due to nail lacquer is fairly common. A case was reported by Miller and Taussig in 1925 [1] and in 1941 Osborne, Jordon and Campbell [2] analyzed a large series. They mentioned the commercial use of identical lacquers for coating such articles as leather handbags, purses, belts, glass beads, wooden and metal jewelry, hairpins, cigaret cases, vanity cases, pens, pencils, broom handles, buttons, straw hats and playing cards. The dermatitis is of the erythematosquamous variety, the upper eyelids, chin, front of the neck and ears being commonly involved, and occasionally the anogenital areas. Thus nail lacquer is an occasional cause of pruritus vulvae. In discussing the paper of Osborne and associates Dr. Ralph Hopkins mentioned the case of a woman who had used nail lacquer to "revive" an old set of earrings; dermatitis of the face and ear lobes had followed. Lacquers of various shades as well as clear lacquer have the same effect in susceptible persons, and the eruption fades in a few days after the lacquer has been removed.

1. Miller, H. E., and Taussig, L. R.: Cosmetics, J. A. M. A. **84**:1999 (June 27) 1925.

2. Osborne, E. D.; Jordon, J. W., and Campbell, P. C., Jr.: Dermatitis Venenata Due to Nail Lacquer, Arch. Dermat. & Syph. **44**:604 (Oct.) 1941.

Recently I observed two cases which point to a new source of nail lacquer dermatitis. Clear nail lacquer is now being used by many women as a coating on costume jewelry, especially metal earrings and necklaces, to prevent discoloration of the skin. By prolonged contact and friction, this lacquer may initiate a dermatitis in women who may have used the same lacquer on their nails for months or years previously without trouble.

REPORT OF CASES

CASE 1.—E. B., a widow aged 49, presented an itching and burning eruption of one week's duration on the ear lobes, sides of the neck and left upper eyelid. In these areas were irregular, sharply outlined, dry erythematous patches with branny scaling. The eruptions had first appeared on the ear lobes while the patient was wearing a pair of silver earrings which she had coated with clear nail lacquer. These earrings had never caused irritation until the lacquer was applied. They had a rather rough surface, which might have scratched the skin. The same lacquer had been used on the nails for some time previously without any trouble. The earrings and nail lacquer were removed, and zinc oxide ointment was applied to the lesions, which disappeared in five days. No lacquer has been used since.

CASE 2.—B. T., an unmarried woman aged 29, showed a pruritic dry scaling erythema of one week's duration all around the base of the neck, and the left upper eyelid and left cubital flexure were similarly involved. The eruption had first appeared about the neck while the patient was wearing a yellow gold necklace which she had coated with clear nail lacquer. This necklace had no rough surfaces and had been worn previously without nail lacquer, with no resulting irritation of the skin. The same lacquer had been used on the nails for a considerable length of time with no ill effects. The necklace and nail lacquer were removed, and zinc oxide ointment was applied to the affected areas, which became clear in six days. The patient is now using a "nonallergic" lacquer on her nails without trouble but has not tried coating her jewelry with it.

SUMMARY

Two cases of dermatitis due to contact with nail lacquer applied to costume jewelry are reported. It is expected that more may be encountered. When they are recognized the jewelry and nail lacquer must be removed and a soothing ointment applied. This procedure constitutes a simple and effective treatment.

316 Michigan Street.

SULFATHIAZOLE SODIUM TREATMENT OF CYSTIC AND INDURATED ACNE LESIONS

A. J. REICHES, M.D.
ST. LOUIS

Danna [1] and Sulzberger and Baer [2] have favorably commented on the use of antibiotic solutions in the treatment of cystic and indurated acne. The use of 5 per cent sulfathiazole sodium seems to give faster and a better percentage of good results. It is my impression that the high p_H of the sulfathiazole sodium has probably helped increase the effectiveness of this method over the use of penicillin.

I began the employment of the technic used in 1942. Best results seem to be obtained by the injection of 5 per cent sulfathiazole sodium directly into the wall of the acne cyst. Great pressure will cause an extrusion of the cyst plug, and results are usually not very effective. The injection of penicillin, which was used almost exclusively during 1945 and 1946, did not in my hands give as effective results as the injection of the aqueous solution of sulfathiazole sodium, and I have returned to the latter.

1. Danna, J. A.: Simple Treatment for Sebaceous Cyst, New Orleans M. & S. J. **98**:5-8 (July) 1945.

2. Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1949, p. 29.

The injection of sulfathiazole sodium around and into the indurated acne lesions followed by the use of hot packs often will give a spectacular result. I have hesitated to add procaine to the solution because of its known effect in minimizing the effectiveness of the sulfonamides.

The drawback in this method is the possibility of sulfathiazole sensitivity. I have, however, been fortunate during this period of eight years in not having had any known case of sensitivity or drug reaction result from the use of this solution.

EXTENSIVE HERPES SIMPLEX: RESPONSE TO AUREOMYCIN THERAPY

WM. F. B. HARDING, M.D.
SACRAMENTO, CALIF.

The response of cutaneous virus infections to aureomycin therapy has been previously reported.[1] The favorable clinical response to topically applied aureomycin in the following case lends further support to accounts of the effectiveness of the drug in a condition for which there has been no specific therapy in the past.

B. M. S., a 30 year old white housewife, acquired symptoms of a common cold, including general malaise and coryza. Within 24 hours a "fever blister" made its appearance on her upper lip beneath the nose. In the past she had experienced an occasional fever blister on the lip during the course of a cold, but in no respect had the lesion been chronic or recurrent. When seen three days after the onset of her fever blister, she had an extensive, severe, erythematous grouped vesicular and papular eruption involving her entire face. On the left side the preauricular lymph nodes were enlarged and tender. There was moderate edema involving the entire face but most pronounced in the orbital areas. The oral temperature was 102 F. The patient was placed on a regimen of rest, the administration of salicylates by mouth, the application of aureomycin ointment to the entire face and the application of solution of aluminum acetate compresses for short periods twice daily. Within three days the temperature was normal and a pronounced involution of the dermatitis on the face had commenced. On the sixth day after treatment was instituted the eruption was entirely cleared.

Although herpes simplex usually runs its course in about a week, in view of its extensive and severe nature in this case it is believed that the aureomycin therapy materially shortened the course of the disease.

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1. Kalz, F.; Prichard, H., and Surkis, S. Z.: Canad. M. A. J. **61**:171 (Aug.) 1949. Bereston, E. S., and Carliner, P. E.: J. Invest. Dermat **13**:13 (July) 1949. Baer, R. L., and Miller, O. B.: J. Invest. Dermat. **13**:5 (July) 1949.

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

Herman Sharlit, M.D., *President*

George M. Lewis, M.D., *Secretary*

Dec. 13, 1949

Linear Psoriasis. Presented by DR. NATHAN SOBEL.

A. R., a woman aged 27, has had typical psoriasis for the past 12 years, involving the elbows, knees, scalp, palms and soles. Six months ago after the birth of a child, a linear eruption developed on the outer aspect of the left thigh, reaching its present extent two months ago.

From the left buttock down the side of the thigh and extending to the anterior aspect of the knee and below it there is a streak consisting of erythematous, scaly papules typical of psoriasis. An eruption between the toes suggesting dermatophytosis is being studied mycologically.

DISCUSSION

DR. MAX SCHEER: The patient might have a psoriasiform linear nevus.

DR. SAMUL M. PECK: I think the diagnosis should be proved histologically, though if I had to make one diagnosis I should say linear psoriasis.

DR. JACK WOLF: I agree with the diagnosis. This disorder is much too characteristic for psoriasis and altogether too diffuse to be confused with linear nevus.

DR. DAVID BLOOM: To me, this linear eruption on the thigh looks like typical psoriasis, and, as the patient has typical psoriasis lesions elsewhere, we can assume with fair certainty that it is also psoriasis. This linear configuration cannot be explained satisfactorily and can only be speculated on, as in the case of lichen striatus.

DR. PAUL GROSS: The bandlike eruption on the left thigh apparently is confined to a metameral segment. Metameral distribution can be observed not only in psoriasis but also in other skin diseases such as morphea or prurigo nodularis.

DR. MAURICE J. COSTELLO: I believe the whole eruption represents psoriasis, that it is psoriasis on the the left buttock and that the disease is in zosteriform distribution. My associates and I presented a little girl—I think before this Society—who had an eruption which corresponds somewhat to this lesion, which was clinically and histologically psoriasis. No lesions of psoriasis appeared elsewhere on the body. The question in this case of a zosteriform eruption is whether the patient received caudal anesthesia, which might have influenced the pattern somewhat.

DR. GEORGE M. LEWIS: The lesions appear to be psoriatic.

DR. HERMAN SHARLIT: How about the patient's having an itch and producing psoriasis?

DR. MAX SCHEER: It is very possibly psoriasis following a scratch mark. Some years ago I read of a little boy who scratched initials on the back of his sister's hand with a pin. The skin was normal in that area, but the girl had typical psoriasis elsewhere. After this trauma psoriasis appeared exactly on the area of the scratch.

A Case for Diagnosis: Tertiary Syphilis? Necrobiosis Lipoidica?
Presented by DR. DAVID BLOOM.

D. A., a woman aged 63, is presented from the Skin and Cancer Unit with ulcers on the right leg, of five months' duration. Just below the right knee are seen three ulcers, one the size of a quarter dollar and punched out, another circinate lesion of similar size and one smaller ulcer above these. All are situated in erythematous skin. There are no subjective symptoms. A similar eruption was present several years ago on the left leg, which now shows a hyperpigmented scar.

Laboratory examinations, including test for blood sugar tolerance, analysis of the urine, and serologic tests for syphilis, all gave normal results except for the observation of 35 mg. per 100 cc. of bromides in the daily urine output.

DISCUSSION

DR. GEORGE C. ANDREWS: Ulcerations are rare in necrobiosis. There is an elevated, somewhat undermined inflammatory border, a history of considerable crusting and a punched-out, deep ulcer. The condition looks more like tertiary syphilis than a bromide eruption, but the latter is a possibility. The patient has a history of pain and tenderness, which is in favor of the latter diagnosis. The serum bromide value is not high enough to mean much. I suspect tertiary syphilis.

DR. MAURICE J. COSTELLO: I would favor tertiary syphilis over necrobiosis also, but there is one thing against that diagnosis. In this case I believe ulceration occurs in the scar, an observation which would be extremely unusual in tertiary syphilis. The lesions on the other leg and the type of healing certainly suggest tertiary syphilis.

DR. HERMAN SHARLIT: Is there ever real healing in necrobiosis?

DR. THOMAS N. GRAHAM: I believe that this patient has tertiary syphilis. The scars on the left leg and their location are quite typical. The favorable response to antisyphilitic treatment also substantiates this diagnosis.

DR. PAUL GROSS: The lesion is suggestive of tertiary syphilis, but if bismuth therapy fails and no other confirmation of the diagnosis can be obtained, the diagnosis of a chronic pyoderma gangrenosum should be considered. Cultures for microaerophilic streptococci could be made. Treatment with zinc peroxide should be instituted if antisyphilitic therapy fails.

DR. JACK WOLF: The eruption did not impress me as being either syphilis or necrobiosis. I suggest that the patient be given aureomycin. In similar instances I have given aureomycin with exceedingly good results.

DR. SAMUEL M. PECK: We have so many drugs which will affect syphilitic lesions and other, nonsyphilitic dermatoses that the therapeutic test cannot be relied on any more. Necrobiosis lipoidica can sometimes be confused with a tertiary lesion because in many respects the pathological processes may be similar. In necrobiosis there is a deposit of lipids in collagenous degeneration. If there should be a patient with a gumma who at the same time has hyperlipemia there can similarly be a deposit of extracellular fat and thus a confusing pathologic picture.

DR. WILBERT SACHS: Clinically, I should have thought of tertiary syphilis. Microscopically, one of the most difficult diagnoses is one involving deep cutis and fat, with large cells such as epithelioid and giant cells. There is necrobiosis in the section, but there are other possible diagnoses, such as dermatitis necrotica, Weber-Christian's disease (panniculitis) and also tertiary syphilis. The presence of giant and epithelioid cells would rule against pyoderma gangrenosum. I believe the vessels should be studied more carefully, for the differential diagnosis between necrobiosis and tertiary syphilis depends entirely on the changes found in them.

DR. GEORGE M. LEWIS: All clinical evidence would seem to point to tertiary syphilis—the location on the upper part of the limb, the punched-out ulcer and the type of scarring. There were no lesions suggesting necrobiosis.

DR. ORLANDO CANIZARES: Dr. Costello's point about the scars is true. I suggest the possibility of atypical Bazin's disease. We have seen several of these cases of tertiary syphilis with negative serologic reactions. Patients with syphilis have been presented who have had negative serologic reactions for a few months and have been statistically classified as cured, who have later manifested tertiary lesions.

DR. NATHAN SOBEL: I have been following this patient irregularly for three or four months. I first saw her when she had had the condition for three or four weeks—a palm-sized, bluish red lesion with an elevated border. I didn't make a definite diagnosis and didn't think the disorder looked like necrobiosis. Recently when I saw the patient again there were three large coin-sized, heavily crusted lesions within this area, an observation which suggested bromoderma; consequently, I had a urine examination for bromides performed. I would favor a diagnosis of tertiary syphilis on clinical grounds.

DR. HERMAN SHARLIT: Dr. Rosen has seen a lot of syphilis, and he said "That is syphilis." The men who saw the slide say the condition is not syphilis. The clinicians say it may be; the histopathologists say it can't be.

DR. DAVID BLOOM: The eruption looked first like bromoderma, and examination of the urine revealed 35 mg. 100 cc. of bromides. Later, because of the punched-out ulcers and circinate lesions which formed below the knee and because of the absence of the color play seen in necrobiosis, the diagnosis of syphilis had to be made. The pathologist insisted, however, that the microscopic picture is that of necrobiosis lipoidica. A therapeutic test with bismuth should help us in the decision.

DR. GEORGE C. ANDREWS: Would the deeper vessels be thickened in necrobiosis?

Chronic Porphyria. Presented by DR. ORLANDO CANIZARES.

A. C., a man aged 47, is presented from the Veterans Adminstration Hospital, Bronx, N. Y., with an eruption of 13 years' duration.

The patient is a construction laborer who first noticed the appearance of bullae on the hands in 1936 at the age of 34. Since that time he has had recurrent crops on the face, neck, arms to the elbows and legs to the knees. He has also acquired blisters under the finger nails with eventual shedding of the affected nail. He has noticed that the skin of the affected areas, with the exception of the legs, has become darker than the rest of the skin. He has not been able to work for the past four years because of the correlation of work with blister formation on the hands. He cannot relate the bullous formation to exposure to sunlight but believes there may be more activity on the face in the summer Although he is often bared to the waist in the summer, the back and chest have not been affected at any time, nor have the elbows, knees, feet, toes or toe nails or any region above the thighs. There have never been any lesions on the mucous membranes.

There is no history of drug ingestion except for occasional taking of ex-lax® (a laxative containing phenolphthalein). The patient has never had any abdominal complaints. He drinks two to three bottles of beer daily. No other member of the family has any skin, abdominal, urinary or central nervous system disorder.

Dark brown pigmentation is present on the face and to the V of the neck, with scattered small crusts and multiple small depressed scars on the face. The V of the neck shows pinkish atrophic scarring. There is dark brown pigmentation of the hands and forearms and scattered crusts on the dorsa of the hands, fingers and forearms. Most of the skin on the dorsa of the hands is atrophic, and there are scattered small atrophic scars on the forearms. A transverse ridge is seen at the distal fourth of each thumb nail, with yellowish dis-

coloration and atrophy of the nail distal to the ridges. There are a few tiny scattered milia on the dorsa of the hands and fingers, and small brownish pigmented and atrophic areas are seen on the anterior tibial surfaces. There are petechiae of the lower third of both legs.

The liver is enlarged 4 fingerbreadths below the right costal margin. The teeth are dirty; they show no reddish fluorescence under Wood's light. An attempt was made to produce bullae by exposure to ultraviolet radiation and by trauma of the left wrist, the left arm just above the elbow, the back and the left calf. The latter two areas received erythema doses. No bullae resulted from these attempts.

The blood count was normal. Various tests and results were as follows: cephalin flocculation, 3+; thymol turbidity, 7.5 units; serum phosphatase, 8.4 units; van den Bergh, (direct) 0.1 and (indirect) 0.6 mg. per cent. The total serum proteins were 8.1, with albumin 4.8 and globulin 3.3 Gm. per 100 cc. The blood cholesterol was 267 mg. per 100 cc. The Kahn and Mazzini reactions were negative.

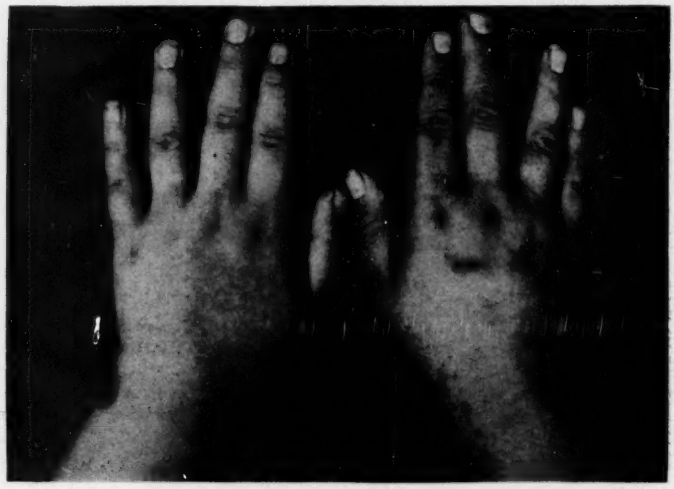

Fig. 1.—Berlock dermatitis due to juice of Persian limes.

The urine was grossly clear, varying in color from normal through light pink to brownish red. There was no change on exposure to daylight or ultraviolet radiation. A reddish fluorescence was seen under Wood's light. On urinalysis increased porphyrins and porphobilinogen were found, but the results were otherwise normal. A 24 hour specimen is now being analyzed for identity and amounts of porphyrins.

Roentgenogram of the chest revealed a number of small rounded calcifications, the largest of which measured about 3 mm., scattered throughout both lungs, which were otherwise clear. The cardiovascular silhouette was normal.

DISCUSSION

DR. MAURICE J. COSTELLO: I agree with the diagnosis as presented. Most of this man's eruption is on the exposed parts of the body, face, neck, lower third of the forearms and hands. The fact that the urine is mahogany colored points to the diagnosis. The unusual feature is that trauma seems to elicit the eruption without exposure.

DR. ANTHONY C. CIPOLLARO: This case belongs to a group that is hard to differentiate. The patient acquired lesions that resemble epidermolysis bullosa or erythema multiforme on exposed parts of the body and shows unusual sensitivity to ultraviolet radiation. There are other factors difficult to ascertain that cause lesions of this type. Because the patient appeared to be mentally retarded, such lesions on the exposed parts of the body might suggest the possibility of pellagra. I think the case deserves study before we can come to a definite conclusion.

Fig. 2.—Berlock dermatitis due to juice of Persian limes.

Bullous eruptions which appear after exposure to the sun are not necessarily due to porphyrins.

DR. PAUL GROSS: I agree with the diagnosis as presented. The scarring of the face would permit the dermatologic diagnosis hydroa vacciniforme. I wonder whether chronic porphyrinuria in this patient could not be the result of liver damage from alcohol and other causes.

DR. DAVID BLOOM: It is important to find out what kind of porphyrins are present in the urine, i. e., coproporphyrins or uroporphyrin. Because of the late appearance of the symptoms, the patient being 47 years of age, and because of the

definite history of liver damage one can assume that in this patient the condition is produced by hepatic disturbance. In these cases one may find sensitivity both to sunlight and to mechanical injury. In cases of hydroa aestivale (vacciniforme) the lesions are found mostly on the nose, ears and backs of the hands, rather than on the legs, as in this case.

DR. GEORGE M. LEWIS: I agree with the diagnosis. It seems to me there is a familial history in some of these cases. Brunsting found a high percentage of liver damage in his cases, and alcoholism was commonly associated.

DR. NATHAN SOBEL: According to the literature, many cases of hereditary porphyria end fatally after attacks of abdominal pain and fever. There are intestinal obstruction and liver failure, for example.

DR. GEORGE C. ANDREWS: I agree that this disorder fits into the group of Brunsting's cases. If the man's liver damage is treated by modern methods, with choline and liver extract, for example, and he is kept from the use of alcohol, it would be interesting to see whether the cutaneous condition responds.

DR. ORLANDO CANIZARES: I think the case belongs to what Dr. O'Leary calls the intermediate or chronic type, which appears late in life because of liver damage. It is true that some cases have a family history, and I shall try to examine members of the family in this case. Dr. O'Leary also mentioned hypertrichosis, but this patient doesn't have that. The liver is definitely damaged. We hope we can make the patient discontinue the use of alcohol, and with medical treatment we might be able to get a better prognosis.

Berlock Dermatitis (Due to Juice of Persian Limes). Presented by DR. PAUL GROSS.

H. B., a girl aged 15, was seen on July 29, 1949, because of brown spots on both hands and forearms.

On July 4 the patient had prepared soft drinks with Persian limes which she had squeezed herself. Shortly after doing so she went into the garden and was exposed to the sun. The following day she noticed red spots and streaks which in a few days turned to their present brown color. She denied having used any perfume or toilet water.

On the right hand are several brown patches, and on the right forearm are brown streaks typical of those caused by running liquid. The left hand shows a diffuse, mottled pigmentation and a dark brown spot on the wrist (figs. 1 and 2).

DISCUSSION

DR. HERMAN SHARLIT: I examined a section from such a case and found deposits of foreign material in the skin, and that was all I saw. This material was in the corium, just as if something were precipitated which gave that color.

A Case for Diagnosis: Lichen Sclerosus et Atrophicus? Idiopathic Macular Atrophy? Syphilitic Macular Atrophy? Presented by DR. THOMAS N. GRAHAM.

METROPOLITAN DERMATOLOGICAL SOCIETY

Joseph C. Amersbach, M.D., *President*
Valentine C. Baker, M.D., *Secretary*
Jan. 16, 1950

A Case for Diagnosis: Erythema Nodosum? Presented by DR. ROYAL M. MONTGOMERY.

E. C., an Italian woman aged 41, has had the present eruption off and on for seven years. She first came to the Skin Clinic of the Hospital for Special Surgery on May 16, 1949.

At the present time there are many red indurated patches on the sides of the legs just above the ankles. They are more prevalent on the outer sides of the legs. All are tender on pressure. There are several single indurated nodules just below the knee. The interdigital webs are macerated and bromhidrosis is present. A roentgenogram of the teeth showed several apical infections. These teeth have been extracted. Ammoniated mercury ointment was prescribed for the toes. The patient has received several courses of sulfadiazine with improvement each time. However, flare-ups have occurred from time to time. Results of urinalysis and complete blood counts have been essentially normal. A biopsy from one of the nodules was "consistent with the diagnosis of erythema nodosum but not suggestive of periarteritis nodosa."

DISCUSSION

DR. VALENTINE C. BAKER: These lesions occur in the winter, and so I was thinking of the possibility of pernio. Sometimes in the winter people will get similar lesions above the ankle. There are vascular changes in pernio.

DR. J. LOWRY MILLER: Clinically this disorder is erythema nodosum. I agree with Dr. Baker that this case seems to be influenced by climatic conditions. The patient has large ankles and probably varicose veins. I would treat her with the application of tight elastoplast® bandages. This procedure is a good treatment for erythema nodosum.

DR. THOMAS N. GRAHAM: I believe that this patient has erythema nodosum. Clinically the eruption is typical of that dermatosis. If this diagnosis is confirmed by microscopic examination, there should be no doubt in regard to the diagnosis.

DR. HARRY VAN VELSOR (by invitation): There was some discussion of the possibility of this being a case of Weber-Christian disease. However, in that condition the lesions are more likely to be on the thighs and produce atrophic areas on resolution. Also, new crops of lesions are usually preceded by variable systemic symptoms. The pathological picture also does not fit Weber-Christian disease. I think the diagnosis of erythema nodosum should be accepted.

DR. CARL T. NELSON: Vascular or erythema-nodosum-like tissue reactions of this type may occur intermittently in hypersensitive persons as an expression of microbial allergy. In this climate, these reactions are related most frequently to nose and throat infections with group A hemolytic streptococci. I suggest, therefore, that throat cultures for streptococci and an antistreptolysin titer, in addition to roentgenograms of the chest, be obtained in this case.

I also have the impression that reactions of this sort may occur as a type of Shwartzman phenomenon. If so, previously sensitized or prepared tissue might respond in this way from time to time as a result of the dissemination of heterologous or nonspecific microbial products from a distant focus. In such cases it is difficult to determine the exact causation but the observation might be used as an argument for the removal of any microbial foci that may be found.

DR. ROYAL M. MONTGOMERY: I do not think this case follows the true course of erythema nodosum. There are crops of erythematous tender nodules. They respond to treatment with sulfadiazine. I shall follow the suggestions which have been made.

A Case for Diagnosis: Psoriasis? Presented by DR. VALENTINE C. BAKER.

A. G., a 48 year old Peruvian man, came to the hospital complaining of low back pains on intercourse. Check-up in the genitourinary department revealed a normal condition. A roentgenogram of the bones of the pelvis showed an excess of calcium. There was a history of treatment for syphilis in 1930 and 1942 for two years.

The patient gives a history of having psoriasis for years. When first seen by me he had a few scaly lesions on the scalp, a small macular lesion with white scales on the glans penis, roughened keratotic lesions on the heels and soles of the feet and yellowish white, broken and friable toe nails. About three weeks ago there appeared two round, slightly raised lesions on the glans penis.

The blood serologic reaction at present is negative. Blood chemistry was as follows: phosphorus, 3.3 mg. per 100 cc.; alkaline phosphatase, 8.8 units, and calcium, 10.9 mg. per 100 cc. Cultures for fungi have been taken.

DISCUSSION

DR. J. LOWRY MILLER: I agree with the diagnosis of psoriasis. The lesions on the penis are of interest. Very often in the absence of lesions of psoriasis elsewhere cases like this are presented as erythroplasia. The lesions here are somewhat smooth and velvety. Many of the cases of erythroplasia which are easily cured are in reality psoriasis.

DR. ROYAL M. MONTGOMERY: I agree with the diagnosis of psoriasis. The man shows two types of psoriatic lesions on the nails. The pittings in the nail plates on the fingers are characteristic of psoriasis. The toe nails show another type of the disease. They are granular and friable. Both observations suggest psoriasis. A culture should be made from the toe nails to rule out a fungous infection. The scaly patches on the heels are unusual. There is little involvement of the skin elsewhere than on the penis.

DR. WILLIAM M. HUBER: It seems to me that psoriasis is the only clinical entity into which all the features of this case fit. I would suggest, however, that the involved nails be given a direct microscopic examination for fungi. We have found in the department of mycology at Vanderbilt Clinic that a diagnosis of fungous infection of the nails can be made much more readily by direct microscopic examination than by culture. We are often unsuccessful in obtaining positive cultures, on the first few trials at least, on nails that are known to give positive results on direct microscopic examination.

DR. THOMAS N. GRAHAM: I agree with the diagnosis of psoriasis. The penile lesions are typical of psoriasis. It is not unusual to find psoriatic patches on the penis without lesions elsewhere on the body. I agree with Dr. Miller that these lesions are sometimes confused with erythroplasia.

DR. HARRY VAN VELSOR (by invitation): I should like to raise a question of therapy. In cases of psoriasis of the nails is it advisable to use spot roentgen irradiation?

DR. JOSEPH C. AMERSBACH: I have had some experience with spot roentgen irradiation. I know that it is successful in some cases and in others is of no value. Similarly, some body lesions will respond to this treatment while others will not. The important factor is to know the clinical type and then carry on trial procedures to determine the best treatment.

DR. J. LOWRY MILLER: In answer to Dr. Van Velsor, I saw a patient who had psoriasis of the nails which did not respond to roentgen ray treatment. Cultures of the nails showed the presence of Trichophyton rubrum. It has been my experience that provided the matrix is not damaged roentgen irradiation usually will help. This man has psoriasis very deep in the nail bed. I do not think roentgen irradiation will help.

DR. ROYAL M. MONTGOMERY: Roentgen ray treatment for the nails is of no value if the dystrophy is caused by T. rubrum.

DR. VALENTINE C. BAKER: I think that psoriasis is probably the proper diagnosis.

NEW YORK DERMATOLOGICAL SOCIETY

John C. Graham, M.D., *President*

Anthony C. Cipollaro, M.D., *Secretary*

Jan. 24, 1950

Plummer-Vinson Syndrome. Presented by DR. MAURICE J. COSTELLO.

E. M., a woman aged 59, of Irish background, born in this country, has been chronically ill for three years but has not been prevented from carrying on her usual activities as a maid. She has been pale and fatigued and complains of painful fissuring of the external canthi, lips and commissures of the mouth. She has also had difficulty in eating, in mastication, in deglutition and in digestion, with alternating constipation and diarrhea. These complaints have been caused by cheilitis, stomatitis, laryngitis, pharyngitis, esophagitis, gastritis and achylia.

The lips are thin and the mouth aperture narrowed, and there is glossitis with magenta color forming a background for the atrophic changes of the glazed mucous membranes. There is loss of vibratory sense in both lower extremities, photophobia, nyctalopia and painful shins.

In spite of the pale appearance (hypochromic anemia), the patient is well nourished.

Treatment has consisted of intramuscular injections of crude liver extract, the vitamin B complex and berubigen (containing 10 micrograms of vitamin B_{12}, preserved with 0.5 per cent phenol, per cubic centimeter).

DISCUSSION

DR. GEORGE M. LEWIS: I presume cultures of the mouth have been made carefully to determine whether monilia is present. Many features of moniliasis are there, and it is difficult to rule that out on clinical inspection alone.

DR. A. BENSON CANNON: I agree with Dr. Lewis' remarks. I am always suspicious of the diagnosis of vitamin deficiency in the case of maids inasmuch as they get the best food.

DR. MAURICE J. COSTELLO: In addition to the other symptoms, the patient also has sensory changes. There was a complete loss of vibratory sensation with the tuning fork on both shins. Her physician said she had a severe secondary anemia. I shall examine the mucous membranes for monilia and report at the next meeting.

Severe Extensive Dermatitis Following Application of Furacin® (Nitrofurazone) Ointment. Presented by DR. HOWARD FOX.

DISCUSSION

DR. J. LOWRY MILLER: When nitrofurazone was first introduced by Downing he found a 5 per cent sensitivity rate. Then, in another series, he found 12 per cent. We consider the use of nitrofurazone inadvisable because of the high rate of sensitivity. At the Marine Hospital we see 1 to 2 cases of nitrofurazone sensitivity a week, largely from prolonged dosage.

Actinomycosis. Presented by DR. A. BENSON CANNON.

J. M., a woman aged 21, consulted the presenter on January 6 because of painless ulcerations of the right cheek and right buttock of five to six months' duration. She has never been out of New York city except for three months at a Florida beach three years ago. Around the first of August a small red papule appeared on the right buttock and a similar one on the back of her right shoulder. The latter healed spontaneously in two months, while the one on the buttock has persisted and slowly enlarged. In October a second

ulceration appeared near the original one on the buttock, and at about the same time the patient noticed a red papule at the angle of the right mandibular area, followed a few days later by a similar lesion in front of the right ear.

Prior to and during the course of the disease the patient was under the treatment of a dermatologist for acne. He opened two papules on the face, thinking they were acne lesions, but the wounds failed to heal and gradually burrowed under the skin, finally connecting in the middle of the jaw in an irregular, linear, elevated formation the size of a lead pencil. Discharging sinuses appeared at intervals along the lesion. Two days prior to the patient's consulting the presenter, a third pea-sized papule appeared in the center of the forehead at the hairline and rapidly became crusted.

During the last several months the patient has been treated at two different hospitals and by several dermatologists in the city with chloramphenicol (chloromycetin®), penicillin injections and sulfonamide drugs, without improvement. Biopsies and numerous cultures were taken, all with negative results.

Examination showed a linear, tortuous, elevated, red, soft swelling extending from the front of the right ear to the side of the chin, measuring 9 by 0.5 to 2 cm. Several sinuses discharged a thin, yellowish gray seropurulent material. On the right buttock there were two oval, red, granular, ulcerated lesions with an undermined, ragged margin. There was a pea-sized, yellowish, heavily crusted lesion on the forehead. On removal of the crust a deep sinus was revealed, undermined for ⅛ to ¼ inch (0.32 to 0.64 cm.). There were three similar pea-sized lesions on the back and on the middle portion of the back of the left thigh.

The Mazzini reaction was negative, and a blood count, results of urinalysis and a roentgenogram of the chest all showed a normal condition. The tuberculin reaction was negative with all dilutions down through 1 : 100. The biopsy showed chronic inflammation and granulation tissue.

Results of mycologic study were as follows: All aerobic cultures were negative. Anaerobic cultures showed gram-positive beaded rods which were nonacid fast, were seen in small clusters and in some instances appeared to branch. These studies are incomplete. The conclusion was that Actinomyces bovis was present.

Treatment has consisted in the administration of 600,000 to 1,200,000 units of procaine penicillin daily and the use of sulfadiazine and aureomycin. The sinuses were opened and curetted and the ulcers and undermined edges swabbed out with 50 per cent phenol. Penicillin ointment was first used, and, later, streptomycin ointment.

All lesions have healed except for two on the buttocks and one on the cheek, and they are slowly clearing up.

DISCUSSION

DR. HOWARD FOX: I recently treated this girl for several weeks. She now has new lesions, and the original ones are larger. I considered actinomycosis as a possible diagnosis because of the location, appearance of the lesions and the patient's contact with a man who had been around horses. Several times I looked for sulfur granules of Actinomyces in the thick pus, without success. Examinations of the blood and urine showed normal conditions. Dr. O. S. Hillman's laboratory reported "large numbers of leukocytes and red blood cells but no evidence of Actinomyces. There were numerous unicellular round structures varying from 15 to 35 microns which did not look like Blastomyces or Coccidioides but could not be identified. Cultures on ordinary mediums and a medium for fungi (Littman's), as well as Petragnani medium (for tubercle bacillus), yielded no growth at the end of 13 days."

Another dermatologist made a diagnosis of dermatitis factitia, and so I employed occlusive dressings for six days and later repeated the procedure, but there was no change. I gave the patient two roentgen ray treatments.

I should like to ask Dr. Cannon whether he saw sulfur granules in the pus.

DR. MAURICE J. COSTELLO: I also saw this patient with Dr. Fox, who certainly was impressed with the possibility of actinomycosis, but we couldn't prove

the diagnosis. The condition is much worse now than it was; the disease is progressing rapidly. Is it the rule for actinomycosis to involve three or four areas within a short period?

DR. ANTHONY C. CIPOLLARO: Why not give aureomycin intravenously?

DR. A. BENSON CANNON: Because the patient is ambulatory.

Tinea Corporis (Trichophyton Crateriforme). Presented by DR. GEORGE M. LEWIS.

A. R., a schoolgirl aged 8, in the early part of December 1949 manifested a scaly, itchy, erythematous circinate eruption on the medial aspect of the right knee. The lesion gradually became larger, and she was seen by a pediatrician at New York Hospital, who made a diagnosis of ringworm and instituted treatment with 5 per cent ammoniated mercury ointment. No cultures were made at that time. One week later the patient had a papular eczematous eruption, which was apparently due to the mercury. This contact dermatitis involved the area of the original lesion and the corresponding area of the left knee. The ammoniated mercury ointment was discontinued and zinc oxide (Lassar's) paste substituted. A mycologic culture was performed December 14 and showed Trichophyton crateriforme. After eight days the dermatitis had cleared and active fungicidal therapy with 3 per cent sulfur and 3 per cent salicylic acid ointment was reinstituted. After a week of insignificant progress the treatment was changed to the use of X-G solution (an experimental antibiotic preparation), and two punch biopsies were taken from the edge and center of the infected area. Cellulitis of these sites interrupted the progress, which has been slow. On Jan. 10, 1950, the therapy was changed to the application of 1.5 per cent iodochlorhydroxyquin (vioform®) in zinc oxide paste, and the lesion is almost clear at present.

It is significant that the patient's playmate has had a fungous infection of the scalp for three months, which condition was finally discovered when the playmate was first seen at the New York Hospital two weeks ago.

The original examination showed a circinate lesion, 3 inches (7.5 cm.) in diameter, with an active border, on the medial aspect of the right thigh and knee.

Tinea Capitis (Trichophyton Crateriforme). Presented by DR. GEORGE M. LEWIS.

M. Q., a schoolgirl aged 5, was first seen in the Dermatology Clinic of New York Hospital on Jan. 9, 1950. Three months previously she had acquired a scaly crusted area on the posterior part of the scalp, accompanied with alopecia. Apparently a fungus had not been suspected because of lack of awareness on the part of her local physician and lack of fluorescence, and no treatment of a specific nature had been given. A culture was reported positive for Trichophyton crateriforme on January 16. A punch biopsy was taken, and sulfur and salicylic acid ointment was applied. No fluorescence was demonstrated under Wood's light.

There is an area of partial loss of hair, 1 inch (2.5 cm.) in diameter, in the occipital area. The involved scalp is erythematous, inflamed and covered with a scaly crust.

DISCUSSION OF CASES OF TINEA CAPITIS

DR. J. LOWRY MILLER: It is important that these cases be pointed out, as we are likely to depend on Wood's light to rule out fungous infections of the scalp.

DR. MAURICE J. COSTELLO: Dr. Frederick Reiss presented from Bellevue Hospital a group of six patients in one family with this involvement.

DR. GEORGE M. LEWIS: The point to emphasize is that this organism is common in Puerto Rico and also around One Hundred and Tenth Street in New York city, where Puerto Ricans are centered. One should keep in mind the possibility of this infection when examining Puerto Rican children. From correspondence with dermatologists in other parts of the country, I gain the impression that this infection has been becoming more prevalent during the last few years.

Malignant Lymphoma. Presented by DR. LESLIE P. BARKER.

A. M., a man aged 56, was first seen by me in September 1949, with an eruption on the left side of the chest, of six months' duration. About a year ago he had a series of "boils" in the same area that were opened in a surgical clinic. The lesions healed very slowly after incision. About six months ago some bluish nodules developed over the area, but the patient is not certain whether they appeared at the exact sites of the previous boils.

Examination showed several lesions just above the left nipple on the anterior wall of the chest, one about 1 cm. in diameter, a second one about 3 by 1.5 cm. and a lower, crescent-shaped lesion about 10 by 2 cm. They were firm, bluish-red elevated lesions that felt cystic in some areas.

Biopsy was performed on the smallest lesion. The nodule was firm, but the center contained a bloody, mucinous material. Microscopic examination showed the epidermis to be intact and of normal appearance. The superficial dermis was thickly fibrous. The remaining dermis and subcutaneous tissue contained large focal and diffuse deposits of lymphoid cells, especially about the sweat gland; the majority of these cells were large lymphoblasts, and a few were of the small lymphocyte type, while others were large basophilic-staining binucleated cells. They varied from the small deeply stained type to the large vesicular type with nucleoli. The diagnosis was malignant lymphoma.

The blood count was normal, and the Wassermann reaction was negative.

The patient was referred to the radiotherapy department for treatment, where he was given 250 r once a week for a total of 2,000 r. Filtration was 0.5 mm. of copper and 1 mm. of aluminum at a distance of 30 cm. using 200 kv. and 10 ma. current.

There was some ulceration during treatment. When this healed, a bluish red elevated lesion still remained in the area. Ten days ago a new large pea-sized nodule appeared near the midline over the sternum. The lesion was excised, and microscopic examination showed "malignant lymphoma." The section taken from the irradiated area failed to reveal any lymphoblastic tissue. General physical examination and repeated roentgenograms of the chest have revealed a normal condition.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I didn't see anything clinically resembling the diseases diagnosed except the healed lesion. Histologically, it was evidently a nondescript type of condition which could only be put in the lymphomatous group of diseases, and members of this group, as is well known, respond to irradiation. This patient received a small dose with excellent involution of all lesions. Whether he will acquire further lesions in the viscera or elsewhere, it is impossible to say.

DR. A. BENSON CANNON: I consider that the patient has not received a sufficient amount of irradiation over a wide enough area to prove effective in a case of sarcoma, which I understand the histologic diagnosis showed the condition to be. The fact that Dr. Barker took a biopsy of the lesion after irradiation because he felt there was still an active process present and also the fact that there has been a recurrence about 2 inches (5 cm.) from the treated tumor force one to believe that the treatment was not adequate. I should have advocated 5,000 r or more and would have irradiated at least 5 to 10 inches (12 to 25 cm.) beyond the tumor growth.

DR. FRANK E. CORMIA: Does Dr. Cannon feel that this syndrome may be fairly localized or that multiple foci of origin may be present? And will roentgen rays, even if administered in a sufficient dose locally, prevent the development of lesions elsewhere in the body?

DR. A. BENSON CANNON: No one can definitely state whether a given lesion represents a primary tumor or metastatic disease. The fact remains that there have been cases of tumors which have apparently been cured by irradiation which have been followed in some instances for almost 20 years after the treatment.

DR. ANTHONY C. CIPOLLARO: Since the entire group of lymphoblastomas responds well to irradiation, I don't see the logic of giving more than enough to produce involution of the lesions we see. Evidently this man has no lesions other than those on the chest. He received a dose of irradiation which produced complete involution of all lesions. More would be superfluous. Whether he is going to acquire any retroperitoneal nodes, no one can say.

DR. A. BENSON CANNON: Lymphosarcomas are usually quite radiosensitive and will disappear with 2,000 r and even with much less. However, they usually continue to make their appearance in or around the irradiated area or in remote portions of the body. I think the physician and the patient have everything to gain and nothing to lose by treating every so-called doubtful case of lymphoblastoma as though it were a malignant lesion. Once the lesion becomes metastatic, the outcome is usually hopeless.

You will remember that the presenter was not sure the tumor had disappeared after irradiation, and so he took a biopsy and later excised a recurrence within or near the irradiated area, which showed sarcoma histologically.

DR. ANTHONY C. CIPOLLARO: When we speak of lymphomas and lymphosarcomas it is not the same as when we speak of squamous cell epitheliomas, which metastasize first to regional lymph nodes. The spread of lymphomas, lymphosarcomas and melanomas is unpredictable. Metastases may appear any place in the body, and therefore all that anyone can do is to treat those lesions that are evident. The prognosis is generally better in those cases in which there is spread by way of the lymphatics.

Recurrent Dermatitis-Herpetiformis-Like Eruption Secondary to Metastases from Uterine Adenocarcinoma (After Hysterectomy). Presented by DR. ANTHONY C. CIPOLLARO.

CLEVELAND DERMATOLOGICAL SOCIETY

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Jan. 26, 1950

Chronic Atopic Dermatitis, with Pronounced Mercury Sensitivity: Partial Clearing After Extraction of Teeth Containing Mercury Amalgam Fillings. Presented by DR. H. H. JOHNSON, DR. I. L. SCHONBERG and DR. NORMAN F. BACH (by invitation).

Mr. A. K., a 32 year old white veteran, was admitted to the Dermatology Service, Crile Veterans Administration Hospital, on Nov. 16, 1949, with the chief complaint of eczematoid dermatitis, present with remissions for six years. He had had eczema in childhood. In 1943 he was hospitalized on three occasions with severe generalized exfoliative dermatitis, occurring each time after contact with metallic mercury with which he worked in a physics laboratory. The same year he had six mercury amalgam fillings placed in his teeth. From 1943 onward he had a constant patch of eczema on the upper lip, and during the final two years of Army service he was hospitalized 15 times in various Army hospitals for treatment of exacerbations of dermatitis on the dorsum of the hands, wrists, antecubital and popliteal spaces and neck. The skin in the perianal region, for a radius of 10 cm., was bright red, vesicular and slightly weeping after a rectal examination in connection with which a lubricant containing 0.02 per cent chloromercuriphenol as a preservative had been used.

On Dec. 3, 1949, the amalgam-filled teeth were extracted, after which operation the patient had an exacerbation of the existing dermatitis and the appearance of vesicles and erythema in both axillas. A week later, his skin began

to clear, according to the patient "faster than it ever had before." A patch test using one tooth and filling was followed by vesiculation, erythema and scaling, which persisted for one week. On December 29 the patient was started on roentgen ray therapy, 75 r two times a week for three weeks, to the wrists, right elbow and neck, and at the time of discharge from the hospital, on Jan. 13, 1950, his skin showed only residual thickening and mild erythema at the sites of previous severe eczema.

DISCUSSION

DR. G. W. BINKLEY: There is no doubt that the patient is sensitive to mercury, and removal of the dental amalgam fillings is of benefit. However, I think the problem still is probably not solved and that the patient may need other treatment for his basic allergies.

DR. H. N. COLE: It is strange that if his dermatitis was due to the mercury —and there is no question about his being sensitive to mercury—there was not more mouth reaction with the amalgam fillings.

DR. H. H. JOHNSON: I think we should give the proper credit to Dr. Louis E. Lieder, an allergist. He is the one who suggested that the fillings might have something to do with the dermatitis and said that he has seen two cases on previous occasions in which there was material relief from the dermatitis after removal of fillings.

MR. J. C. TOWER: Has BAL (2,3-dimercaptopropanol) been tried?

DR. G. H. CURTIS: I wonder whether or not this case could be properly classified as atopic dermatitis. It is true that when the patient was a child he had had a dermatitis on his cheeks, but he had had no further trouble with the skin until he apparently was sensitized to mercury. I think this condition could be classified as a fixed eruption from mercury rather than an atopic dermatitis, in spite of its distribution.

DR. H. H. JOHNSON: The use of BAL has been disappointing in this type of case, in which one is dealing with a sensitivity rather than an acute intoxication.

A Case for Diagnosis: Reticuloendotheliosis? Presented by DR. I. L. SCHONBERG.

S. U., 17 months of age, has had a skin eruption since he was 4 weeks of age. At the onset the infant had a "cradle cap," which gradually spread over the skin of his face and about the ears. A scaly red process then developed on the back, abdomen, crural folds and buttocks. The palms and soles were involved early in the process. These were dry, scaly and somewhat thickened.

At 5 months of age the child was admitted to University Hospitals because of frequent bouts of diarrhea. At that time it was noted that there had been since birth a laryngeal stridor, both inspiratory and expiratory. It was also noted that the infant did not follow light well and that there were wandering motions of the eyes at all times. There was also evidence of impaired hearing.

This baby was the first child of a 23 year old woman, who had been well throughout pregnancy. Labor had been 27 hours long, and the delivery had been spontaneous. There was no jaundice and no cyanosis. The infant breathed well at birth. At the age of 5 months he had doubled his birth weight.

The family history is noncontributory.

The patient is a well developed, well nourished child, with a severe inspiratory stridor. Over the scalp, face, ears, trunk and extremities there is an erythemato-squamous process. On the scalp there is some crusting and "piling up" of scales. In some areas, particularly in the folds, there is fissuring, with slight exudation. There is thickening and scaling of the palms and soles. The eyes present normal pupils and eyegrounds. There is a wandering type of nystagmus, and little attempt is made to follow light. The ears, nose and throat are normal. The liver edge is 3 fingerbreadths below the right costal margin. The spleen is at the left costal margin. The lymph nodes are generally enlarged.

A roentgenogram of the chest made on June 2, 1949, showed slight widening of the upper mediastinum but an otherwise normal condition. A roentgenogram of the long bones showed thickening of the periosteum in the femur, tibia and humerus. A roentgenogram of the skull revealed no abnormality.

A bone marrow smear was normal. Results of urinalysis were normal. A hemogram showed 65 per cent hemoglobin, 3,540,000 red blood cells and 17,700 white blood cells, with 65 per cent neutrophils, 32 per cent lymphocytes and 3 per cent monocytes. The total lipids were 290, the cholesterol 102 and lecithin 230 mg. per 100 cc. Observations on spinal fluid examination were normal.

A lymph node was excised on Jan. 25, 1949, with a report of melanosis.

A definite diagnosis was not reached at the time of the patient's discharge from the hospital, but a possibility of reticuloendotheliosis was entertained.

DISCUSSION

DR. B. P. PERSKY: I felt that the erythematous scaly appearance suggested congenital ichthyosis.

DR. H. H. JOHNSON: I agree with Dr. Persky, and I think the fact that this condition was bad in the first winter of the child's life and almost completely cleared up in the summer, to become worse in the winter, would support that diagnosis in contrast to one of reticuloendotheliosis.

DR. G. A. DEOREO: I agree with the diagnosis of ichthyosis, but I think there is something in addition. The color of this child's skin certainly suggests an infiltration with some fatty substance, and whether or not there is a single diagnosis which would explain the dermatological defects exhibited I am not prepared to say.

DR. H. N. COLE JR.: I noted the striae which are present. It is rather difficult to explain the entire picture with one diagnosis. Certainly the cerebellar involvement, the nystagmus and the stridor could go along with reticuloendotheliosis. The possibility that the yellow desquamation of the skin might indicate carotene rather than infiltration with any other substance must be considered. Unfortunately, we do not have films here, but thickening of the periosteum is described. If there is any actual involvement of the bones from reticuloendotheliosis, I think it would show more the picture of osteoporosis. I think that infiltration of lipid substance would give the picture of osteoporosis rather than thickening of the periosteum. I am inclined to think that the bone changes are not related to the skin involvement.

DR. I. L. SCHONBERG: The diagnosis of congenital ichthyosis, as well as of a member of the reticuloendotheliosis group, was considered as a possibility. In the literature, particularly in articles by Layman and Sweitzer, a great deal has been said about the type of rash in reticuloendotheliosis. The observations in this case are consistent with that diagnosis.

Folliculitis Ulerythematosa Reticulata; Granulosis Rubra Nasi? Presented by DR. M. BRODY.

The patient, R. S., aged 26, has a pitted, worm-eaten appearance of the skin of the malar area of the face. He states that he has never had acne except for an occasional papule on the chin and forehead. He denies having had any other skin disease involving the cheeks.

The patient also has an erythema of the nose associated with sweating. He states that when it is cold outside his nose is the coldest part of his body and that when he is warm his nose becomes very warm. In 1946 a dermatologist diagnosed the condition as granulosis rubra nasi. Treatment of the nose as for rosacea, with dilute hydrochloric acid, brewer's yeast and sulfur lotions, did not produce an appreciable improvement.

The patient has seven brothers and one sister. He states that two brothers have this condition. I saw one of the brothers, who did have a mild involvement of the cheeks. Neither the brothers nor the sister is prematurely gray.

The reaction to the Kline test was negative. The red blood cell count was 4,800,000, and the white cell count, 7,200. Permission for a biopsy was refused.

DISCUSSION

DR. H. HECHT: The term folliculitis ulerythematosa reticulata should be reserved for a certain form of lesion. This name was proposed 70 or 75 years ago for lesions which start with erythema on the outside of the eyebrows and later have ulceration. No other areas are affected.

As to the second diagnosis, that of granulosis rubra nasi, that condition is a disease of children. I never read about or saw it in adults. I have always taught students that if they find something that looks like psoriasis, in 95 per cent of the cases it is psoriasis. In this case I would say that the disorder is psoriasis. People who spend a lot of time outdoors have such red noses. My diagnosis would be psoriasis.

DR. H. J. PARKHURST: This is a condition that MacKee described as folliculitis ulerythematosa reticulata, and I felt that the scarring on the left cheek was fairly characteristic of that condition. I could not accept the nasal eruption as granulosis rubra nasi. It suggested to me seborrhea congestiva, which might put one in mind of a possible lupus erythematosus. I feel that the patient should be kept under observation for that possibility.

DR. I. L. SCHONBERG: I too felt that this was a typical case of folliculitis ulerythematosa. In a person of the patient's age it is possible that the amount of atrophy is diminished.

DR. M. BRODY: We presented this case as a rare entity regarding the folliculitis ulerythematosa. The other diagnosis was made by a dermatologist in Pittsburgh. I also believe that several lesions are not as evident today as they were a couple of years ago, when I first saw the patient.

Demodicidosis (Demodex Infestation of the Scalp). Presented by DR. H. G. MISKJIAN.

H. P., aged 53, had an eruption of the scalp of three weeks' duration. For some time past he had felt a little soreness of the scalp and had used an ointment, which gave him relief. Mr. P. stated that he had had no other skin diseases except "psoriasis" some 35 years ago; this had completely cleared up.

The patient is a tall, thin man with a bald scalp. There is a faint, diffuse redness all over the top of the head, where the hair is altogether absent. On this red or purplish red background one sees, on close examination, a large number of very small, intensely red, more or less acuminate papules, not larger than 1 or 2 mm. in diameter. Most of them have a white top the size of a pinpoint. These papules or papulopustules represent the primary element characteristic of Demodex infestation. To prove it, one has only to open the top of one of them, mix with a drop of immersion oil some of the clear, oily liquid which can be easily squeezed out with a little pressure and examine the preparation under low power. This procedure revealed numerous Demodices in this case.

The patient's face is completely clear; it is not flushed.

DISCUSSION

DR. B. LEVINE: This has not been described anywhere in the textbooks.

DR. B. P. PERSKY: Does Dr. Levine mean that Demodex has never been found or that it has never been found on the scalp?

DR. B. LEVINE: That it has never been found on the scalp.

DR. J. H. STRAUCH: When I was in the Navy I happened to treat a Red Cross nurse who had large cystic lesions on the face, from almost every cyst of which 12 or 15 of these Demodex organisms could be expressed. I prescribed benzyl benzoate locally, and, much to my surprise, the lesions cleared up almost completely. I tried it in subsequent cases without results.

DR. H. G. MISKJIAN: I have two reasons for presenting this case. The first is that the condition must be rare, because this is only the second case I have seen in more than 10 years. The second reason is that it is not described in books. I have not gone over the journals, but I have looked over the standard books in three languages and have found nowhere a description of anything resembling it.

I saw my first patient with this disorder in 1938. He was a bald man in his fifties. He had an eruption on his scalp composed of small red, discrete papules, almost identical with those observed today. I called it a simple folliculitis and gave the patient some ammoniated mercury ointment. He came to me for two or three months, without having much improvement, and then dropped out of sight. In 1941 his condition was still the same. During the interim, however, my attention had been called to the importance of the role played by Demodex in the production of lesions of the skin, especially on the face, in acne rosacea. I had found the primary element characteristic—I am tempted to say almost pathognomonic—of Demodex infestation and had learned to identify it. In looking over the man's scalp this time, I recognized immediately the characteristic primary element produced by Demodex, that small red follicular papule. The secretion obtained by squeezing two or three of these papules revealed an abundance of Demodex organisms. I prescribed the use of an ointment containing 10 per cent sulfur and 5 per cent peruvian balsam. In a week the patient telephoned to say that he was cured.

Since then I have been on the lookout, but it was not until three or four weeks ago that I came across my second case, that of the man you saw today. In order to preserve the lesions for this meeting, I gave him some coal tar–ammoniated mercury ointment.

Another syndrome I have been able to ascribe to the presence of Demodex is an eruption on the face which resembles a dermatitis and almost invariably is diagnosed as a contact dermatitis. I have seen several of these eruptions, all on young women. My first case I called a contact dermatitis and got nowhere treating it until one day, a month or so after the beginning of treatment, I perceived a number of tiny conical papules, not very red, which aroused my suspicion. Sure enough, they contained Demodex. With fear in my heart I prescribed the application of 10 per cent sulfur ointment and saw the eruption respond very rapidly to this treatment. Recently I saw a medical secretary who had the same type of eruption on the face. A very careful search for the cause of her contact dermatitis had revealed nothing, and the condition was not responding to treatment. She had the characteristic tiny papules, and in those papules there were a good many Demodices. The response to sulfur and peruvian balsam ointment, applied with caution, was almost immediate. It took a good deal of time, however, to clear up the disorder completely.

These observations lead me to think that we may be missing an important cause of skin trouble by overlooking the possible pathogenic role of Demodex folliculorum.

Pustular Psoriasis. Presented by DR. H. H. JOHNSON, DR. I. L. SCHONBERG and DR. NORMAN F. BACH (by invitation).

Congenital Syphilis, Syphilitic Osteitis and Osteomyelitis. Presented by DR. B. LEVINE and DR. E. L. GLICKSBERG.

A Case for Diagnosis: Lichen Ruber Moniliformis? Presented by DR. N. R. KRUPKIN (by invitation), DR. I. L. SCHONBERG and DR. B. LEVINE.

Pityriasis Rubra Pilaris. Presented by DR. GEORGE H. CURTIS.

Periadenitis Mucosa Necrotica Recurrens. Presented by DR. R. G. NORBY and DR. R. F. SPILLER (service of DR. H. H. JOHNSON and DR. I. L. SCHONBERG).

DETROIT DERMATOLOGICAL SOCIETY

Frank Stiles, M.D., *President*

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Jan. 11, 1950

Psoriasis and Deep Mycotic Infection (Sporotrichosis, Disseminated Ulcerating Type)? Presented by DR. THOMAS H. MILLER.

Mrs. H. W., a white woman aged 52, acquired a tender nodule on the anterior surface of the left leg four years ago. A diagnosis of carbuncle was made by her physician, but the lesion did not heal. Gradually a patch of dermatitis developed which is still present in spite of much treatment including the maximum amount of roentgen irradiation permissible. Later a similar lesion developed on the upper part of the back. This ulcerated, formed a draining sinus and healed, leaving a scar. Similar lesions have continued to develop on the chest and back up to November 1949. In October 1949, the patient acquired red scaly plaques on the extensor surfaces of the elbows and the hands as well as thickening of the nails of the hands and feet and thick keratotic lesions on the soles.

The patient was first seen in November 1949, and a biopsy was taken from a node on the right side of the chest. This was reported by Dr. Hermann Pinkus as showing chronic granulomatous inflammation, and the diagnosis of sporotrichosis was suggested, with other deep mycotic infections or syphilis as alternatives. The blood Kahn test gave negative reactions. Culture of seropurulent material from a closed node on the chest showed only contaminants on Sabouraud's medium. Treatment with potassium iodide was instituted and resulted in considerable improvement.

At present there are numerous partly erythematous scars on the chest and back. The extensor surfaces of the elbows are covered with red plaques which are covered with a loose white scale. The hands show similar lesions which are undergoing involution. Most of the finger nails have been desquamated.

DISCUSSION

DR. HENRY A. BRUNSTING, Toledo, Ohio: The psoriatic lesions do not seem to be active. Could the other lesions be pyodermic granuloma? The condition is a severe systemic one.

DR. EDWARD P. CAWLEY, Ann Arbor, Mich.: If this patient had sporotrichosis, a therapeutic test with the iodides would be of help in making the diagnosis. Sporotrichosis responds to treatment with iodides better than do any of the other deep mycoses.

DR. THOMAS H. MILLER: The patient has been receiving potassium iodide therapy, which evidently not only has healed all the subcutaneous lesions but has given the patient a great sense of well-being.

DR. HERMANN PINKUS, Monroe, Mich.: The biopsy showed chronic granulomatous inflammation. Because of the general characteristics of the tissue reaction and the absence of stainable organisms in the sections I suggested the diagnosis of sporotrichosis. I am wondering whether one could explain all the lesions which this patient presents—abscesses, psoriasiform plaques and nail involvement—on the basis of a monilia infection.

DR. THOMAS H. MILLER: I believe that this patient has two conditions, a sporotrichosis of the unusual, widespread, subcutaneous variety and psoriasis.

DR. ARTHUR E. SCHILLER: All the nails show the same age and advancement of the disease; they would not if the condition were a fungous infection.

DR. EDWARD P. CAWLEY: I have never seen a case of sporotrichosis with nail destruction. I believe the disorder is psoriasis plus something else.

DR. DONALD BOERSMA, Grand Rapids, Mich.: Hidradenitis suppurativa should be considered in the differential diagnosis. The negative cultures and the cordlike scarring are compatible with hidradenitis suppurativa. Aberrant apocrine glands are sometimes seen on the back and chest. This diagnosis does not explain the other dermatological observations.

DR. HENRY A. BRUNSTING, Toledo, Ohio: It would be unusual to find apocrine glands on the back.

A Case for Diagnosis: Nevoxanthoendothelioma? Reticulogranuloma?
Presented by DR. HERSCHEL S. ZACKHEIM, Royal Oak, Mich. (by invitation).

P. K., a 7 month old white girl, presents a generalized papular eruption. The lesions are hard dark red papules scattered over the trunk, extremities and scalp. One is on the left side of the tongue, and there are a few about the vulva. Some of the lesions have apparently involuted, leaving dark brown pigmented macules. A few bright red lesions may be found which are only slightly infiltrated and may represent the earliest stage of development. The lesions measure up to 0.5 cm. There is no splenomegaly, hepatomegaly or lymphadenopathy.

The first lesions were noted on the chest when the child was at the age of 5 months. New lesions have continued to appear since that time, but quite a few older lesions have undergone involution, leaving only pigmentation. They are apparently asymptomatic. No urtication can be produced. The baby's general health has been good.

Examination of the blood showed red blood cells, 5,600,000, and hemoglobin, 10 Gm., for a color index of 0.7. There was poikilocytosis and anisocytosis. There were 7,800 white blood cells, of which 22 per cent were polymorphonuclear cells, 76 per cent lymphocytes, 1 per cent monocytes and 1 per cent basophils. Serum cholesterol was 163.3 mg. per 100 cc. (normal). Roentgenologic examination of chest and skull showed no abnormalities.

Microscopic examination of a papule from the upper part of the back was reported as follows (Dr. Hermann Pinkus): "The epidermis was almost normal. The corium contained masses of large pale-staining cells, partly in nodes and partly infiltrating between the connective tissue bundles. The infiltrate was present in all layers from the subcutis to the papillae, and occasional cells were found in the epidermis. The protoplasm of many of the cells appeared vacuolated, but no true foam cells were seen. There were a few mitoses and a considerable number of multinucleated giant cells. Eosinophilic leukocytes were scattered in the corium. Numerous red blood cells were present everywhere between the large cells, and in some places the impression was gained that one was dealing with incompletely formed blood vessels. In other places well formed vessels with intact walls ran within the masses of large cells. The general impression was more that of a granuloma than that of a tumor. The possibility or reticulogranuloma was considered, but, because of the many giant cells and the vacuolization of the cells, a diagnosis of nevoxanthoendothelioma was suggested. The clinical diagnosis of hemangioendothelioma could not be confirmed."

DISCUSSION

DR. HENRY A. BRUNSTING, Toledo, Ohio: I believe that nevoxanthoendothelioma is the diagnosis in this case.

DR. EDWARD P. CAWLEY, Ann Arbor, Mich.: The presence of eosinophils in the section suggests the possibility of this condition's being a type of eosinophilic granuloma. Many people believe that eosinophilic granuloma is related to Letterer-Siwe disease.

DR. HERMANN PINKUS, Monroe, Mich.: The section showed histiocytic infiltrate and a number of giant cells. That observation was the reason for suggesting

nevoxanthoendothelioma. No fat stains were done yet. The possibility of the Letterer-Siwe type of reticulogranuloma was considered, but the clinical picture does not seem to bear out that diagnosis.

DR. ARTHUR E. SCHILLER: What would be the relation of this disorder to nevic showers?

DR. HERMANN PINKUS, Monroe, Mich.: Nevic showers remain. Some of these lesions have faded.

DR. ARTHUR E. SCHILLER, I have seen nevi come and go.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: I believe this case belongs in the group of Letterer-Siwe and Hand-Schüller-Christian diseases.

DR. LOREN W. SHAFFER: The lesions of this child have changed decidedly in color in the last week. They were bright red; now many are brown.

DR. FRANK STILES, Lansing, Mich.: Is any treatment indicated?

DR. COLEMAN MOPPER (by invitation): The usual involuting course of nevoxanthoendothelioma varies from six months to three years in duration, and certainly some of the lesions have changed in character within the past two weeks, since I first saw this patient.

DR. ARTHUR C. CURTIS: The lesions seem to be involuting now.

NOTE.—Several later biopsies showed no lipid contents; neither did they show so many giant cells. The diagnosis of benign reticulogranuloma therefore appeared more likely.

Dermatofibroma (Dermatofibrosarcoma Protuberans?). Presented by DR. JAMES R. DELANEY.

N. R., a white man 41 years of age, noticed a small area of numbness on his back 20 to 25 years ago. About 10 years ago three small nodules developed in the medial border of the lesion. These slowly enlarged and coalesced to form the tumor mass which is present now. There never has been any pain or discomfort.

Examination shows a firm brownish red intracutaneous plaque in the region of the left scapula. The lesion measures 7 by 9 cm., is slightly elevated and shows at the lateral border a group of nodules which measure from 1 to 1.5 cm. in thickness.

Two biopsies were taken, one from a nodule and the other one from the opposite border of the plaque, and were reported by Dr. Hermann Pinkus as follows: "This was a fibromatous lesion. The one biopsy showed a diffuse increase of fibroblasts between the connective tissue bundles. There was some new formation of fine collagenous fibers between the preformed bundles. The upper part of the corium was edematous and showed widened lymph spaces and a small number of inflammatory cells. These changes might have been due to obstruction of lymph channels in the deeper layers. The other biopsy represented the fully developed picture. In it the connective tissue bundles were separated by numerous newly formed fine fibers and slender bundles of collagen with many spindle cells. This process was taking place diffusely throughout the corium. The epidermis was slightly hypertrophic, and the appendages were undergoing atrophy. The changes appeared benign, but in the second biopsy there was a certain resemblance to the more fibrotic parts of those lesions which are known as dermatofibrosarcoma protuberans."

DISCUSSION

DR. LOREN W. SHAFFER: We have seen at the City of Detroit Receiving Hospital three patients within the last three months with dermatofibrosarcoma protuberans. This condition is quite rare, and it is unusual that we have seen so many examples in such a short time. The condition is considered to be benign but subject to local recurrence unless totally excised. For this reason it has been classified under the descriptive term progressive and recurrent dermatofibrosarcoma.

Metastases have been reported, however, in several cases by Binkley (Binkley, G. W.: Dermatofibrosarcoma Protuberans: Report of Six Cases, ARCH. DERMAT. & SYPH. **40**:578, 1939). Dr. Mopper and Dr. Pinkus are reporting our first two cases in the *American Journal of Clinical Pathology* (**20**:171-176 [Feb.] 1950).

DR. COLEMAN MOPPER (by invitation): This tumor clinically appears as a dermatofibrosarcoma protuberans but certainly is not as typical as those which are being reported from the Receiving Hospital. I feel that this case has given me further insight into the clinical appearance of dermatofibrosarcoma, as this tumor has a broad infiltrating intracutaneous base or foundation, which acts as a supporting structure for subsequent protuberant growth. I have seen three other cases of this nature, besides the one presented today, and all presented the shelflike foundation. Thus, I firmly believe that Dr. Delaney's case is compatible with the picture of dermatofibrosarcoma, but its exuberant nature is not as pronounced as in the other cases I have seen.

DR. HERMANN PINKUS, Monroe: Histologically, this case stands at the benign end of the spectrum which this peculiar group of dermatofibrosarcoma presents. Highly cellular lesions, indistinguishable from spindle cell sarcoma, are at the other end. These biopsies were particularly interesting to me in comparison with dermatofibroma lenticulare (histiocytoma). The process in Dr. Delaney's case is much more insidious and diffuse, and there was none of the whorl formation and localized proliferation of cells which characterize the "nodulus cutaneus." Hematoxylin and eosin sections were disappointing because they showed nothing but a slight increase of apparently normal fibroblasts. It was only the connective tissue and elastic fiber stains which gave full realization of the pathologic process.

Fixed Drug Eruption Due to Phenolphthalein. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

Chronic Disseminated Lupus Erythematosus with Violent Pruritus. Presented by DR. GEORGE VAN RHEE and Dermatological Staff of Harper Hospital.

Subacute Disseminated Lupus Erythematosus. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

A Case for Diagnosis: Chronic Granuloma. Presented by DR. GEORGE VAN RHEE and Dermatological Staff of Harper Hospital.

Rheumatoid Arthritis and Juxta-Articular Gouty Nodes (Uric Acid Crystals Demonstrated). Presented by DR. GEORGE VAN RHEE and Dermatological Staff of Harper Hospital.

Lichenoid Tuberculid. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

Urticaria Pigmentosa, Juvenile Type. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

Universal Psoriasis. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

Ehlers-Danlos Syndrome plus Granuloma Annulare. Presented by DR. ARTHUR E. SCHILLER and DR. HERBERT H. HOLMAN.

Acarophobia. Presented by DR. G. B. SEXTON, London, Ontario, Canada.

A Case for Diagnosis: Porokeratosis Mibelli? Linear Keratotic Nevus? Presented by DR. DAVID KAHN, Lansing, Mich.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

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Jan. 20, 1950

Parapsoriasis en Gouttes. Presented by DR. PAUL FASAL.

Resistant Impetigo? Dermatitis Factitia? Presented by DR. REES B. REES and (by invitation) DR. EDWIN M. HAMLIN.

Erythema Induratum? Presented (by invitation) by DR. W. J. COLE.

Leishmaniasis Americana (Ear Ulcer of the Chicleros). Presented by DR. ALEXANDER GRADOW and DR. PAUL FASAL.

Toxic Vasculitis (Erythema Annulare Centrifugum?) Presented (by invitation) by DR. RALPH BEHLING and DR. JAMES MCGINLEY.

Acroscleresis. Presented by DR. EUGENE FARBER.

News and Comment

GENERAL NEWS

Laboratory Training Courses.—Courses to be given during 1951 at the United States Public Health Service Communicable Disease Center, Chamblee, Ga., will include Laboratory Diagnosis of Syphilis (February 12 to 23 and March 12 to 23); Microbiology for Public Health Nurses (February 26 to March 2); Laboratory Diagnosis of Bacterial Diseases, General Bacteriology, Part 1 (February 26 to March 9) and Part 2 (March 12 to 23); Laboratory Diagnosis of Parasitic Diseases, Part 1, Intestinal Parasites (March 5 to 23) and Part 2, Blood Parasites (March 26 to April 13), and Laboratory Diagnosis of Enteric Diseases, Part 1, Introductory Enteric Bacteriology (March 26 to 30). Information concerning the courses to be given during the remainder of the year and application forms may be secured from the Officer in Charge, Laboratory Training Services, Communicable Disease Center, United States Public Health Service, Post Office Box 185, Chamblee, Ga.

Opening for Full Time Training at University of Illinois.—There is an opening available for full time training in dermatology and dermatological research at the University of Illinois College of Medicine under the supervision of Drs. Francis E. Senear and Adolph Rostenberg Jr. The candidate will be accepted for a minimum of two years. Inquiries should be addressed to either Dr. Senear or Dr. Rostenberg.

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For the general information of indexers, catalogers and library personnel with reference to the listing of the new title of this journal, we advise that the *Quarterly Cumulative Index Medicus* policy be followed. The *Quarterly Cumulative Index Medicus* with its volume 49 (January-June 1951) will list this journal under the new title, so that the letters A. M. A. will be included as an integral part of the title. For the completion of volume 48 (July-December 1950) the *Quarterly Cumulative Index Medicus* will continue to use the old title, without adding the designation A. M. A.

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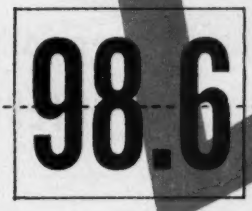
Bibliography (1) Hewitt, W. L., and Williams, Jr., B.: New England J. Med. *242*:119, 1950. (2) Recinos, Jr., A.; Ross, S.; Olshaker, B., and Twible, E.: New England J. Med. *241*:733, 1949. (3) Wood, E. J.: Lancet *2*:55, 1949.



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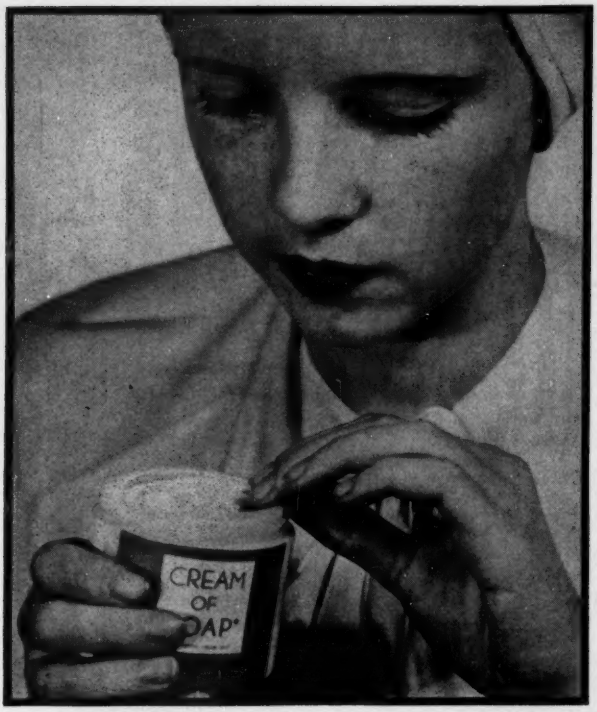

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1 Gross, Elmer R., M.D.; Wright, Carroll S., M.D.; Oral Bismuth Therapy in Syphilis and Various Dermatoses—Paper presented at the Pennsylvania Medical Society Meeting, October 8, 1946 at Philadelphia, Pennsylvania.

2 Gross, Elmer R., M.D.; Howles, James K., M.D.; Non-Specific Treatment of Dermatoses and Adjunctive Therapy of Syphilis with Oral Sodium Bismuth Triglycollamate. Read before the Section of Dermatology and Syphilology Meeting of the Centennial Meeting of the A.M.A. at Atlantic City, New Jersey, June 12, 1947.

3 Year Book of Dermatology and Syphilology, 1946, page 31.

4 Sawicky, H. H., M.D.; Bistrimate (sodium bismuth triglycollamate) Administered by Mouth in the Treatment of Chronic Discoid Lupus Erythematosus. The Journal of Investigative Dermatology, vol. 9 #3 September 1947.

5 Howles, James K., M.D.; Treatment of Inflammatory-Dermatoses with Oral Bismuth (sodium bismuth triglycollamate). Southern Medical Journal, vol. 41 #11, pages 1033-1041, November 1948.

6 Pascher, Frances, M.D.; Sawicky, H. H., M.D.; Silverberg, M.G., M.D.; and Emmet, Richard, M.D.; Bistrimate for Lupus Erythematosus, Lichen Planus and other Dermatoses. Journal of Investigative Dermatology, vol. 10, #6, June 1948.

7 Miller, Thomas H., M.D. and Delaney, James R., M.D.; Oral Bismuth therapy in Dermatology. Archives of Dermatology and Syphilology, Vol. 60, August 1949.

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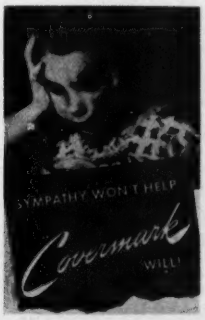

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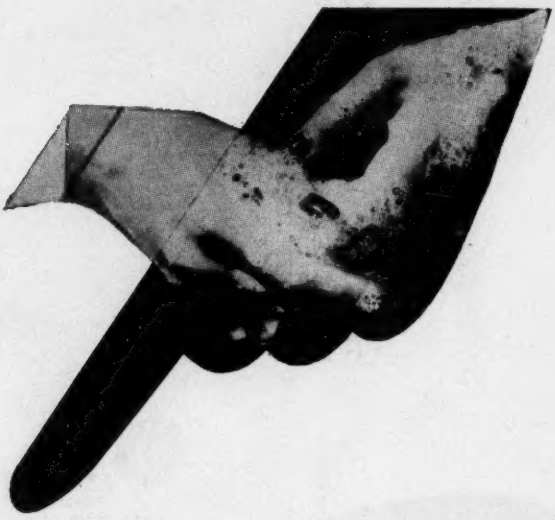

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